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PASSMEDICINE

HEMATOLOGY & ONCOLOGY

Internal medicine

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PASSMEDICINE PART 2

HEMATOLOGY

2024

Question 1 of 191

A 40-year-old woman attends the emergency department with sudden onset abdominal pain. She feels nauseated and has vomited 4 times in the past 2 hours. Her past medical history includes hypothyroidism and vitiligo.

On examination, she has a temperature of 38.2ºC. She has a heart rate of 135bpm with a blood pressure of 116/66mmHg. There is guarding and tenderness on palpation of her right iliac fossa. Rovsing's sign is positive. It is noted that she has mild bruising and petechiae over her back and extremities and on further questioning, she tells you she has been suffering from frequent nosebleeds over the past 2 weeks.

She is reviewed by the general surgical team who want to prepare her for theatre. Investigations:

Hb	127 g/L	Male: (135-180)Female: (115 - 160)
Platelets	28 * 10 /L 9	(150 - 400)
WBC	15.2 * 10 /L 9	(4.0 - 11.0)
Na +	136 mmol/L	(135 - 145)
K +	4.1 mmol/L	(3.5 - 5.0)
Urea	5.6 mmol/L	(2.0 - 7.0)
Creatinine	87 µmol/L	(55 - 120)
Prothrombin time (PT)	11 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	26 secs	(25-35 secs)
Fibrinogen	2.1 g/L	(2 - 4)
D-Dimer	275 ng/mL	(< 400)
CRP	60 mg/L	(< 5)

What is the next step in this patient's management?

A. Intravenous immunoglobulin
B. Plasma exchange
C. Platelet transfusion
D. Prednisolone
E. Romiplostim

A. Intravenous immunoglobulin

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

This patient has immune thrombocytopenic purpura (ITP) the immune-mediated destruction of platelets. It is more common in older females and those with a history of autoimmune disease. It may present as easy-bruising, petechiae or epistaxis or may be an incidental finding on routine blood tests as seen here. The first-line treatment of choice is oral prednisolone. However, in patients who do not respond to or have contraindications to prednisolone use or those who require a rapid rise of platelets (for example, prior to having surgery) then intravenous immunoglobulin (IVIG) can be given. This patient requires a rapid rise of platelets due to her urgent surgery for likely appendicitis making IVIG the more appropriate choice in this scenario.

Plasma exchange is not a treatment for ITP. However, it is the treatment of choice for thrombocytopenic thrombotic purpura (TTP) a rare acquired disorder of coagulation that is associated with fever, acute kidney injury, central nervous system dysfunction (including confusion, seizures or coma), thrombocytopenia and microangiopathic haemolytic anaemia.

Platelet transfusion is a treatment of choice in ITP. However, it is typically reserved for cases of an acute haemorrhagic event or cerebral haemorrhage. As this patient is otherwise well with only evidence of minor bleeding, it would not be the first-line treatment of choice.

Romiplostim is a thrombopoietin receptor agonist which is a 3rd-line agent to treat ITP. It is considered in patients who have not responded to 1st and 2nd line treatment or have symptoms of chronic ITP persisting for beyond 12 months.

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A 50-year-old gentleman presents with fatigue and bruising to the emergency department. On examination, hepatosplenomegaly is noted, but no peripheral lymphadenopathy is palpable. The following blood tests are obtained:

Hb	73 g/l
Platelets	43 * 10 /l9
WBC	2.3 * 10 /l9
Neutrophils	0.8 * 10 /l9
Lymphocytes	1.3 * 10 /l9
Monocytes	0.0 * 10 /l9
Basophils	0.02 * 10 /l9
Eosinophils	0.1 * 10 /l9

He is diagnosed with hairy cell leukaemia.

Which gene is mutated in this malignant condition?

A. BRCA1
B. BRAF
C. TP53
D. NOTCH1
E. HER2

B. BRAF

BRAF is mutated in hairy cell leukaemia

Hairy cell leukaemia is caused by a mutation in exon 15 of the gene for the protein kinase BRAF. Patients may be asymptomatic with the disease is identified incidentally or present with symptoms of cytopenia.

The most common laboratory finding is cytopenia, usually affecting two or three lineages. Leucocyte counts tend to be low, with a monocytopenia present in 90% of patients. Hairy cells are often seen in peripheral blood films but their proportion is variable. They have a characteristic appearance; lymphocytes with villous cytoplasmic projections, oval nuclei and finely mottled pale grey-blue cytoplasm.

A germline mutation in BRCA1 underlies an increased risk of malignancy (especially breast and ovarian) seen in some families. This gene is also mutated, as a somatic mutation, in other cases of breast and ovarian cancer.

A germline mutation in TP53, encoding tumour suppressor protein p53, underlies Li Fraumeni syndrome. However, p53 is mutated in over 50% of malignancies, the most commonly mutated protein. Activating mutations in NOTCH1 are implicated in T cell acute lymphoblastic leukaemia and the HER2 gene is amplified in some forms of breast cancer. These are somatic mutations.

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A 59-year-old woman presents to the haematology clinic for review. Despite treatment with cyclophosphamide, rituximab and fludarabine (FCR), she has experienced a steady rise in her lymphocyte count, accompanied by symptomatic anaemia. Examination reveals evidence of anaemia, her body mass index is 22 kg/m², and there is obvious splenomegaly.

Which of the following is the most appropriate intervention?

A. Ibrutinib
B. Lapatinib
C. Everolimus
D. Pazopanib
E. Sunitinib

A. Ibrutinib

Ibrutinib is effective and can be used for the treatment of CLL in patients who have failed a previous therapy

Ibrutinib is a small molecule kinase inhibitor which binds to Bruton's tyrosine kinase which is involved in B cell clonal replication. It therefore has an important role in the treatment of B cell malignancies including mantle cell lymphoma and chronic lymphocytic leukaemia (CLL). It is recommended for patients who have had at least one previous therapy for CLL or those with a 17p deletion or TP53 mutation.

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A 76-year-old gentleman with myelofibrosis is found to have a haemoglobin of 67 g/l on admission. He is transfused two units of red cells and discharged home three days later. Six days later, he is readmitted febrile and jaundiced. Blood tests show:

Hb	71 g/l	Na +	137 mmol/l	Bilirubin	39 µmol/l
Platelets	97 * 10 /l 9	K +	3.9 mmol/l	ALP	82 u/l
WBC	2.8 * 10 /l 9	Urea	4.9 mmol/l	ALT	15 u/l
Neuts	1.5 * 10 /l 9	Creatinine	79 µmol/l	Albumin	26 g/l

What is the most appropriate management for this condition?

A. Prednisolone
B. Intravenous immunoglobulin
C. Conservative management
D. Packed red cells
E. Tazocin

C. Conservative management

A delayed transfusion reaction occurs 7-10 days after the transfusion

This is a delayed transfusion reaction, which typically occurs 7-10 days post-transfusion. It occurs when patients are sensitised from previous transfusions or pregnancy and have alloantibodies against red cell antigens which are not picked up by cross-matching, if below detectable limits.

Management includes informing the laboratory and sending a repeat group and save sample for further testing. Usually, supportive management is sufficient, though if symptomatic from anaemia, they may require further transfusion after the further crossmatching testing is carried out. Prednisolone and intravenous immunoglobulin are not used in this situation typically. If this were bacterial contamination of the blood product, tazocin would be appropriate, though this presentation is too late and there are no other signs of sepsis.

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A 44-year-old woman is referred to ambulatory care with a 10-day history of lethargy and exertional dyspnoea. Prior to this episode, she reports having mild coryzal symptoms that have since settled. Her past medical history is only significant for hypothyroidism which is well controlled on levothyroxine.

A full screen of blood tests is sent:

Hb	71 g/L	(135 - 180)
Platelets	110 * 10 /L 9	(150 - 400)
WBC	7.0 * 10 /L 9	(4.0 - 11.0)
Urea	6.3 mmol/L	(2.0 - 7.0)
Creatinine	110 µmol/L	(55 - 120)
Prothrombin time (PT)	11 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	26 secs	(25-35 secs)
Fibrinogen	3.1 g/L	(2 - 4)
D-Dimer	345 ng/mL	(< 400)
Reticulocytes	2.5 %	(0.5 - 1.5)
Blood film	Schistocytes	
Coombs test	Negative	
Bilirubin	59 µmol/L	(3 - 17)
ALP	128 u/L	(30 - 100)
ALT	40 u/L	(0 - 40)
AST	50 u/L	(< 35)
Blood glucose	5.2 mmol/L	(4 - 7)
Total cholesterol	7.1 mmol/L	(< 5)

What is the most likely diagnosis?

A. Autoimmune haemolytic anaemia
B. Disseminated intravascular coagulation
C. Paroxysmal nocturnal haemoglobinuria
D. Thrombotic thrombocytopenia purpura
E. Zieve syndrome

A. Zieve syndrome

Zieve syndrome is a rare clinical syndrome of Coombs-negative haemolysis, cholestatic jaundice, and transient hyperlipidaemia

This patient has a likely diagnosis of **Zieve syndrome** given the triad of non-autoimmune haemolysis, jaundice and hyperlipidaemia. The negative Coombs test indicates non-autoimmune haemolytic anaemia. In Zieve syndrome, jaundice can be cholestatic in nature but also secondary to haemolysis. The raised ALP supports a cholestatic picture. Zieve syndrome is a rare syndrome and generally resolves following the cessation of alcohol use.

Autoimmune haemolytic anaemia is incorrect. Although there is evidence of haemolysis given the low Hb, reticulocytosis, raised bilirubin and presence of schistocytes, the Coombs test is negative. A negative Coombs test makes autoimmune haemolytic anaemia very unlikely.

Disseminated intravascular coagulation (DIC) is incorrect. DIC is a disease of abnormal coagulopathy characterised by a prolonged prothrombin time, prolonged APTT, low fibrinogen and a very high D-dimer. Triggers for DIC include malignancy, surgery and significant infection of which none are mentioned in this presentation. The resolved coryzal symptoms are unlikely to be significant.

Paroxysmal nocturnal haemoglobinuria (PNH) is incorrect. PNH is characterised by intravascular haemolysis, bone marrow hypoplasia and increased risk of thromboses. This does not completely fit the patient's presentation making this answer incorrect.

Thrombotic thrombocytopenia purpura (TTP) is incorrect. This condition presents as a pentad of fever, acute kidney injury, thrombocytopenia, microangiopathic haemolytic anaemia and cerebral dysfunction. The absence of the majority of these features makes TTP unlikely.

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A 54-year-old gentleman is admitted under the medical team with a diagnosis of urosepsis. Twenty four hours after admission he develops numerous bruises across his abdomen, arms and legs. It is also noted that he is bleeding from his cannula site

His blood results are as follows

Hb	110 x10 /L 12	130-168 x10 /L12
WCC	19 x10 /L 9	4.2-10.6 x10 /L9
Platelets	50 x10 /L 9	130-370 x10 /L9
CRP	300 mg/L	0-5 mg/L
Fibrinogen	3.8 g/L	1.8-4.0 g/L
PT	20s	9-12s
APTT	38s	23-31s
Creatinine	150µmol/L	60-125 µmol/L
eGFR	60 mL/min/1.73 m 2	>90 mL/min/1.73 m2

What is the most likely cause?

A. Idiopathic thrombocytopenia purpura (ITP)
B. Thrombotic thrombocytopenia purpura (TTP)
C. Disseminated intravascular coagulation (DIC)
D. Heparin induced thrombocytopenia (HIT)
E. Haemolytic uraemia syndrome (HUS)

C. Disseminated intravascular coagulation (DIC)

In DIC fibrinogen can be normal or elevated in over 50% of cases especially early on (as fibrinogen is an acute phase marker)

Fibrinogen is an acute phase marker. Therefore in DIC fibrinogen levels can be normal or elevated in over 50% of cases especially early on.

PT/APTT are usually normal in ITP, TTP, HUS and HIT

Renal function is markedly abnormal in HUS

In HIT the plasma prothrombin time (PT) is decreased but the activated partial thromboplastin time (aPTT), and the fibrinogen levels are normal.

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You are called to see a 68-year-old female on the oncology ward who has developed coffee ground vomiting. She has a diagnosis of colorectal cancer which she is currently undergoing curative chemotherapy for.

Blood results are as follows:

Hb	95 g/l
Platelets	34 * 10 /l9
WBC	14 * 10 /l9
PT ratio	2.4
aPPT ratio	2.1
D-dimer	1540 ng/ml (normal < 500)
Fibrinogen	0.8 g/l (normal 1.5-4.0)

You administer fresh frozen plasma. Repeat blood results are as follows:

Hb	91 g/l
Platelets	24 * 10 /l9
WBC	18.4 * 10 /l9
PT ratio	2.2
aPPT ratio	1.9
Fibrinogen	0.85 g/l (normal 1.5-4.0)

What treatment is indicated?

A. Cryoprecipitate
B. Vitamin K
C. Factor VIII
D. Factor IX
E. No further treatment

A. Cryoprecipitate

In bleeding patients with DIC with severe hypofibrinogenaemia (<1 g/l) that persists despite FFP replacement, then fibrinogen concentrate or cryoprecipitate is indicated

The patient has DIC likely secondary to malignancy. In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful. Notably, this patient continues to have severe hypofibrinogenaemia despite administration of FFP. In bleeding patients with DIC with severe hypofibrinogenaemia (<1 g/l) that persists despite FFP replacement, then fibrinogen concentrate or cryoprecipitate is indicated.

Vitamin K would be indicated in Vitamin K deficiency. There is nothing in the history to suggest vitamin K deficiency.

Factor VIII and factor IX are indicated for Haemophilia A and B respectively.

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A 74-year-old woman is referred to the medical assessment unit with diffuse bone pain affecting her back and ribs that has persisted for two months. She has no significant past medical history and is not on any regular medications. She does not smoke and still workers as a potter.

Clinical examination is unremarkable and there are no focal areas of tenderness or swelling. There is no organomegaly or lymphadenopathy. Cardio-respiratory examination is unremarkable.

Blood tests:

Hb	111 g/L	Male: (135-180)Female: (115 - 160)
Platelets	389 * 10^9 /L	(150 - 400)
WBC	4.2 * 109 /L	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	4.8 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	10 mg/L	(< 5)
Calcium	2.68 mmol/L	(2.20-2.60)
Immunoglobulin G	24.1 g/L	(6.6 - 15.9)
Immunoglobulin A	4.4 g/L	(0.6-5)
Immunoglobulin M	2.2 g/L	(0.53 - 2.47)

Serum protein electrophoresis:

Paraprotein	present

Given the likely diagnosis, what is the first-line imaging investigation?

A. Isotope bone scan
B. Low dose whole body CT
C. Fluorodeoxyglucose positron emission tomography CT (FDG PET-CT)
D. Plain radiographic skeletal survey
E. Whole body MRI

A. Whole body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

Whole-body MRI is the correct answer. This patient presents with diffuse bone pain, anaemia, hypercalcemia, raised IgG and a paraprotein. She likely has multiple myeloma. Recent NICE guidelines state that imaging should be offered to all patients with suspected myeloma and that whole-body MRI is the first-line choice in the absence of contraindication.

Low dose whole-body CT is incorrect. This investigation can be offered if an MRI is contraindicated or not tolerated.

A plain radiographic skeletal survey is incorrect. This is only offered if CT or MRI are unsuitable or not tolerated.

Isotope bone scan is incorrect. This is not recommended in the investigation of suspected myeloma.

FDG PET-CT is incorrect. This imaging investigation is only an option for those patients with confirmed multiple myeloma who have not yet had any whole body imaging

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A 67-year-old man with a previous diagnosis of myelodysplasia presents to a haematology clinic with rapid weight loss, an increase in nosebleeds and a greater feeling of fatigue than previously. He has the single lineage dysplasia subtype and usually requires monthly transfusions; he has presented two weeks after his last red blood cell top-up.

His blood results are as follows:

Hb	66 g/L	Male: (135-180)Female: (115 - 160)
Platelets	9 * 109 /L	(150 - 400)
WBC	1.1 * 109 /L	(4.0 - 11.0)

A blood film is sent for and he is admitted for blood and platelet transfusions.

What is the blood film likely to show?

A. Burr cells
B. Fragmented red blood cells
C. Lymphoblasts
D. Myeloblasts
E. Smear cells

D. Myeloblasts

Myelodysplasia may progress to acute myeloid leukaemia

Myeloblasts is the correct answer as this is most likely a malignant transformation of myelodysplasia to acute myeloid leukaemia (AML). This is evidenced by the myeloblasts coupled with the significant drop in haemoglobin, platelets and white blood cells, with the B symptoms of weight loss and fatigue becoming more prominent. The clue in the blood tests is that he previously had single lineage dysplasia which causes refractory anaemia, but now he has platelet and white blood cell reduction indicating bone marrow failure. The white cells overproduced in AML are the immature myeloblasts, not normally found in the blood.

Burr cells are incorrect as these are spiculated red blood cells commonly found in chronic renal failure due to high levels of nitrogen in the blood destabilising the red cell membrane.

Lymphoblasts are incorrect as these cells are only found in the peripheral blood film in acute lymphoblastic leukaemia.

Smear cells are incorrect because they are the result of artefactual damage to mature lymphocytes during film production, often characteristic of chronic lymphoblastic leukaemia.

Fragmented red blood cells are seen in many conditions which result in intravascular haemolysis, such as renal failure, microangiopathic haemolytic anaemia, haemolytic uraemic syndrome or thrombotic thrombocytopenic purpura. The reason for the anaemia, in this case, is bone marrow failure as opposed to haemolysis.

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An 18-year-old woman presents to the haematology clinic with spontaneous bruising, heavy periods and recurrent epistaxis. This has been a continuous problem during her teenage years but she was recently found to have anaemia and received an iron transfusion which prompted further investigation into these symptoms.

On examination, she is well and alert. There are numerous purpura across both arms and she denies trauma or any itchiness.

Hb	98 g/l
Platelets	314 * 10 /l9
WBC	5.6 * 10 /l9
PT	13.8
APTT	34.3
PFA-100 assay	prolonged closure time
Flow cytometry	GPIIb/IIIa negative
Ristocetin-induced platelet aggregation	normal agglutination

What is the likely diagnosis?

A. Bernard-Soulier disease
B. Glanzmann thrombasthenia
C. Von Willebrand disease
D. Haemophilia A
E. Evan's syndrome

B. Glanzmann thrombasthenia

Innate defective glycoprotein IIb/IIIa -> Glanzmann's thombasthenia

This is a test of the coagulopathies. Von Willebrand disease and haemophilia tend to have raised APTT. Evan's syndrome is an autoimmune disease with low platelets and red blood cells. The PFA- 100 assay shows that platelets are not aggregating and this may be due to platelet glycoproteins or their interaction with von willebrand factor. The ristocetin effectively allows aggregation of von willebrand factor to GPIb and does not require GPIIb/IIIa. Therefore Glanzmann thrombasthenia will have normal platelet aggregation once ristocetin is added.

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A 48-year-old man was admitted to the acute medical unit with history of haematemesis and melaena. No previous history was available. He required fluid resuscitation and had eight-units of red cell transfusion. On review after his transfusion, his pulse was found to be 80 beats per minute and blood pressure 130/78mmHg. Chest and abdominal examination were essentially normal. Repeat bloods were taken and results are as shown below:

Hb	110g/l (130 - 180)
Platelets	80 * 10 /l (150 - 400)9
WBC	10 * 10 /l (4.0 - 11.0)9
Prothrombin time	14.2secs (11.5 - 15.5)
INR	1.3 (<1.4)
APTT	32secs (30 - 40)
Thrombin time	17secs (15 - 19)
Fibrinogen	2.1g/l (1.8 - 5.4)

Which blood product should he be given at this stage?

A. Cryoprecipitate and fresh frozen plasma
B. Fresh-frozen plasma
C. Fresh-frozen plasma and platelets
D. Platelets
E. No blood products are indicated

A. No blood products are indicated

Fresh frozen plasma is offered to bleeding patients who have either a prothrombin time or activated partial thromboplastin time greater than 1.5 times normal

Decisions on transfusion of blood products should recognize that over-transfusion may be as damaging as under-transfusion by exposing patients to the risk of fluid overload and other complications of transfusion. Do not offer platelet transfusion to patients who are not actively bleeding and are haemodynamically stable. Platelets may be given to those actively bleeding and have a platelet count of less than 50 Ã— 109/L. Offer fresh frozen plasma to bleeding patients who have either a prothrombin time or activated partial thromboplastin time greater than 1.5 times normal; and cryoprecipitate or fibrinogen concentrate to those with a fibrinogen level of less than 1 g/L. Offer prothrombin complex concentrate to patients who are taking warfarin and actively bleeding. Treat patients who are taking warfarin and whose upper gastrointestinal bleeding has stopped in line with local warfarin protocols.

Question 12 of 191

A 65-year-old man has been admitted with worsening abdominal pain, hypotension and altered mental state. He is currently being treated for intra-abdominal sepsis secondary to peritoneal dialysis for chronic renal failure secondary to diabetic nephropathy. Previous medical history includes type 2 diabetes mellitus, angina, hypertension, hyperlipidaemia, and diabetic retinopathy. The patient is not anti-coagulated but does take aspirin.

He is started on intravenous antibiotics and intravenous fluid. His results are:

Hb	91 g/L	Male: (135-180)Female: (115 - 160)
Platelets	60 * 10^9 /L	(150 - 400)
WBC	24.5 * 10 /L 9	(4.0 - 11.0)
Na +	128 mmol/L	(135 - 145)
K +	5.8 mmol/L	(3.5 - 5.0)
Urea	31.7 mmol/L	(2.0 - 7.0)
Creatinine	645 µmol/L	(55 - 120)
CRP	317 mg/L	(< 5)
PT	22 seconds	(10-14 seconds)
APTT	56 seconds	(30-40 seconds)

He undergoes a CT scan which shows a spontaneous retroperitoneal haemorrhage and is referred to interventional radiology.

Given the patient's coagulation profile, what blood product is needed?

A. Cryoprecipitate
B. Fresh frozen plasma
C. Protamine
D. Prothrombin complex concentrates
E. Recombinant activated factor 7

B. Fresh frozen plasma

In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful

Fresh frozen plasma is correct. The clinical picture above is that of DIC. There is a prolongation of both PT and APTT. Patients with disseminated intravascular coagulopathy go through a hypercoagulable state followed by a hypo-coagulable state as they use up their reserves of clotting factors. Fresh frozen plasma replaces multiple clotting factors. The disturbed clotting state, as shown with prolongation of PT and APTT, indicates that clotting factor concentrations are below 30% of normal. A typical dose of fresh frozen plasma (15ml/kg) will increase circulating clotting factors by 10%.

Cryoprecipitate is incorrect because this is used to replace fibrinogen in haemorrhaging patients. It also contains Factor VIII and XIII, von Willebrand's Factor and fibronectin. It can be used in patients with von Willebrand's disease and haemophilia.

Protamine is incorrect because this is used to correct the effects of heparin, either unfractionated heparin or low molecular weight heparin. Administration can cause hypotension and high doses can inhibit platelet function.

Prothrombin complex concentrate is incorrect because this is used to reverse warfarin and can be used to reverse some direct oral anticoagulants. This includes clotting factors II, VII, IX and X. It is used for the rapid correction of an acquired coagulation disturbance, commonly warfarin. PT levels are monitored for dose-response. Repeat doses may be required 8-12 hours after the initial dose. An example is Octaplex.

Recombinant activated factor 7 is incorrect because this is used in haemophilia patients and off label in severe multiple trauma, non-traumatic intracranial haemorrhage and some surgeries. It is almost identical to native factor 7.

Question 13 of 191

A 45-year-old man is admitted from a local park. On arrival, he is in respiratory distress with a ventilatory rate of 34 breaths per minute and a peripheral oxygen saturation of 89% on 15L/min oxygen via a non-rebreathe mask. He is grey and sweaty with central cyanosis. Heart rate is 122bpm and blood pressure is 94/66mmHg. Examination of the chest discloses a normal cardiorespiratory examination and there is no clinical indication of heart failure. A chest x-ray shows no acute pathological lesion but background emphysematous changes and an ECG shows only sinus tachycardia with a corrected QT interval approaching the upper limit of normal with no ischaemic lesions.

An arterial blood gas taken on 15L/min oxygen shows:

pH	7.17	HCO3-	13.4	Glucose 6.9 mmol/l	MetHb	35%
pO2	10.9	Base excess	-5.8	Potassium 5.5 mmol/l	COHb	8%
pCO2	6.7	Lactate	4.1 mmol/l			

He is beginning to show signs of tiring and confusion and his GCS has fallen to 13/15 (E3V4M6) but he tells you he has been inhaling Liquid Gold (an alkyl nitrite).

Which of the following interventions is most appropriate in this patient's immediate management?

A. Continuous positive airways pressure ventilation (CPAP) pending transfer to a hyperbaric chamber
B. Reduce inspired oxygen concentration and controlled oxygen therapy via Venturi valve
C. 75mg 1% methylthioninium chloride solution IV over 5 minutes
D. 300mg 3% sodium nitrite solution IV over 10 minutes
E. 50ml 8.4% sodium bicarbonate solution IV over 20 minutes

D. 75mg 1% methylthioninium chloride solution IV over 5 minutes

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe3+ (ferric) to Fe2+ (ferrous)

The arterial blood gas in the above clinical description shows a mixed respiratory and metabolic acidosis with a relative hypoxia despite the inspired fraction of oxygen. However, the significant abnormality is the fraction of methaemoglobin on the gas at over 30% which is significantly elevated. The carboxyhaemoglobin level is slightly raised at 8% but levels such as this may be seen in smokers and are not necessarily pathological. In this case, the diagnosis is of acute methaemoglobinaemia which is a rare but potentially fatal consequence of inhalation of poppers (alkyl nitrites).

Poppers are a clear or yellowish, sweet-smelling volatile liquid which is inhaled as a recreational drug of abuse which yields euphoric and anxiolytic effects. It also is a vasodilator and is sometimes used as an adjunct in sexual acts, and previously was a treatment for angina pectoris. However, in some patients, particularly susceptible individuals such as those with sickle cell traits or a G6PD deficiency, inhalation of poppers may rapidly oxidise ferrous iron ions in haemoglobin to their ferric (Fe3+) states creating methaemoglobinaemia (MetHb). MetHb binds oxygen more avidly than haemoglobin and causes a shift in the dissociation curve to the left meaning that oxygen is not liberated in the tissues causing a cellular hypoxia. This manifests in a clinical cyanosis and often a deathly grey pallor to the patient. Oxygen saturations may not be as shocking as the patient appears since many pulse oximeters cannot distinguish between oxyhaemoglobin and methaemoglobin well. However, supplemental oxygen will not improve recorded values (although it should still be given). An impairment in gas exchange is often seen in acute methaemoglobinaemia with raised tensions of CO2 and low tension of O2 and consequent respiratory acidosis. An additional metabolic acidosis occurs due to cellular anoxic respiration. In smokers, this condition may be mistaken for a type 2 respiratory failure due to chronic obstructive lung disease. The methaemoglobin count and low bicarbonate make this unlikely and reducing the inspired oxygen is likely to worsen the situation. CPAP may be tried but will not reverse the underlying problem and hyperbaric oxygen is helpful only in situations of high carboxyhaemoglobin, such as carbon monoxide poisoning, which is not the case here.

The first line treatment for methaemoglobinaemia is the administration of methylthioninium chloride, also known as

methylene blue, which reduces the ferric ions back to their ferrous states rapidly. Several administrations may be required, especially in high concentrations of MetHb. Sodium nitrite is a recognised treatment for cyanide poisoning. It actually causes methaemoglobinaemia since cyanide ions are cleared more rapidly when complexed with MetHb. Administration of sodium nitrite is not indicated in this vignette and will make the situation worse. Sodium bicarbonate may well be indicated in this patient due to the profound acidosis but it is not the most pressing concern. Rectification of the oxygen-carrying capacity of the blood may improve the acid-base balance without the need for bicarbonate, and hypoxia is likely to kill the patient more quickly than acidosis with a normal potassium. Remember that 8.4% bicarbonate solution, if given, should ideally be infused through a central vein since it is extremely caustic.

Question 14 of 191

A 74-year-old gentleman presents with shortness of breath on exertion. He denies cough, wheeze, or chest pain. He has a past medical history of Hodgkin's lymphoma. Examination of the cardiopulmonary system is normal.

Blood results are as follows:

Hb	55 g/l
Platelets	346 * 10 /l9
WBC	8.4 * 10 /l9

You decide to transfuse him two units of red cells. What special request will you make?

A. Leukodepleted
B. CMV negative
C. No special request required
D. Irradiated red cells
E. Cell salvage

D. Irradiated red cells

The risk of transfusion associated graft versus host disease in Hodgkin's lymphoma is unrelated to the treatment modality and/or disease stage. Individuals with Hodgkin's lymphoma should therefore receive X- or gamma-irradiated blood for life

If an immunocompromised patient receives red cells that are not irradiated, the donor's T cells can cause transfusion-associated graft-versus-host disease (TA-GvHD), in which the donor T lymphocytes mount an immune response against the recipient's lymphoid tissue causing tissue and organ damage, potentially leading to death.

Typical clinical features of TA-GvHD include fever, an erythematous maculopapular rash, abdominal pain and profuse diarrhoea.

Irradiation of blood products destroys the donors T lymphocytes thereby helping to prevent this potentially fatal complication.

Indications for gamma irradiated blood products include:

- Immunocompromised marrow or organ transplant recipients
- Patients with haematological disorders who will be undergoing allogeneic marrow transplantation imminently
- Intrauterine transfusions
- Patients with Hodgkin's disease
- Patients treated with purine analogue drugs (e.g. fludarabine)

Interestingly, the risk of transfusion associated graft versus host disease in Hodgkin's lymphoma is unrelated to the treatment modality and/or disease stage. Individuals with Hodgkin's lymphoma should therefore receive X- or gamma-irradiated blood for life.

In the UK, all blood products are leukodepleted to prevent Creutzfeldt-Jakob disease transmission.

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates

Question 15 of 191

A 28-year-old woman presents to the acute medical unit with fatigue, lethargy, and abdominal pain. She is pregnant at 32 weeks gestation.

Blood results are as follows:

Hb	62 g/L	Male: (135-180)Female: (115 - 160)
Platelets	182 * 10 /L 9	(150 - 400)
WBC	8.8 * 10 /L 9	(4.0 - 11.0)

You discuss the case with the obstetrics registrar on call who advises you that they will review the patient in the department and asks you to arrange a blood transfusion.

What special red cell requirements are required?

A. Cytomegalovirus (CMV) negative
B. High titre anti-A and anti -B negative
C. Irradiated
D. Leukodepleted
E. Washed

A. Cytomegalovirus (CMV) negative

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates

Cytomegalovirus (CMV) negative is the correct answer. CMV is a type of herpes virus. Primary infection is usually asymptomatic but may cause a flu or glandular fever-like illness, leading to a lifelong infection in all age groups. The virus resides in monocytes and can reactivate from its latent state. More severe disease may occur in individuals with impaired immunity such as foetuses, neonates and patients of any age who have been immuno-suppressed by disease or treatment.

Transmission of CMV present in blood components can give rise to primary infection in CMV negative patients or to reinfection in previously infected patients.

With very few stated exceptions (e.g. granulocytes), from November 1999 all allogeneic blood components produced in the UK have been subjected to a leukocyte depletion process. This was primarily a vCJD risk reduction measure, however, it has resulted in other added benefits including reduced incidence of non-febrile haemolytic transfusion reactions, TRALI, and transfer of CMV.

The following groups of patients require **CMV-negative blood**:

Intra-uterine transfusions

Neonates up to 28 days post expected date of delivery Pregnancy

As the patient in this clinical case is pregnant, CMV-negative blood is required.

Historically, immunocompromised patients who have not been infected with CMV (CMV negative) received CMV-negative blood due to the possible life-threatening complication of infection. However recent studies have shown that leukodepletion is just as effective as CMV IgG-negative blood components. Therefore CMV IgG negative donations are no longer required in this cohort.

Irradiated blood is required in individuals with severe immunodeficiencies, those with a history of Hodgkin's lymphoma, patients who have been exposed to certain drugs (e.g. bendamustine and fludarabine), and following stem cell transplant. Pregnancy is not an indication for irradiated blood.

All blood products in the UK are **leukodepleted** (with very few exceptions eg granulocytes). This is therefore not a special requirement.

With transfusion of plasma-rich components (e.g. FFP and platelets), we are more concerned about the passive transfer of antibodies (e.g. Anti-A and Anti-B) in contrast to the transfer of antigens as in red cell transfusions (which contain negligible amounts of plasma). Thus for plasmarich components, group AB is the universal donor and group O is the universal recipient, in stark contrast to packed red cells. **High titre anti-A and anti -B** negative can be requested for incompatible plasma-rich transfusion. This clinical case is regarding red cell transfusions and thus this special requirement is not applicable.

Washed red cells can be requested for patients who have recurrent febrile or allergic reactions to standard packed red cells. Pregnancy is not an indication for washed red cells.

Question 16 of 191

A 35-year-old man presents to the emergency department with generalised weakness, nausea, and joint pain. He has a past medical history of depression for which he has been prescribed sertraline but has not taken it for several months. He is a current smoker and also uses intravenous recreational drugs.

On examination, he has a non-blanching, slightly raised purplish rash over his torso and part of his limbs. He is slightly jaundiced and has mild right upper quadrant tenderness.

Blood tests are taken:

Bilirubin	51 µmol/L	(3 - 17)
ALP	188 u/L	(30 - 100)
ALT	142 u/L	(3 - 40)
Î³GT	82 u/L	(8 - 60)
Albumin	29 g/L	(35 - 50)
HBsAg	Negative	
Anti-HBV	Negative	
Anti-HCV	Positive	
HCV RNA	Positive	
HIV antibodies	Negative	

What is the most likely diagnosis?

A. Cold agglutinin disease
B. Cryoglobulinaemia type 1
C. Cryoglobulinaemia type 2
D. Cryoglobulinaemia type 3
E. Warm autoimmune haemolytic anaemia

C. Cryoglobulinaemia type 2

Hepatitis C + purpuric rash → cryoglobulinaemia

This patient, in summary, has generalised weakness, arthralgia, and a rash consistent with palpable purpura on the background of a diagnosis of hepatitis C. The combination of hepatitis C and purpura is suspicious of cryoglobulinaemia. Meltzer's triad is a combination of palpable purpura, arthralgia, and weakness and are the classical symptoms of cryoglobulinaemia.

There are three types of cryoglobulinaemia. It is **cryoglobulinaemia type 2** that is associated with hepatitis C and therefore this is the correct answer. Other associations of type 2 include rheumatoid arthritis, Sjogren's, and lymphoma.

Cold agglutinin disease is an autoimmune disease caused by the presence of cold-sensitive antibodies which act on red blood cells. It has both primary and secondary forms, of which hepatitis C can be a trigger of secondary cold agglutinin disease. Symptoms can include arthralgia and weakness, but the presence of palpable purpura is not associated. Therefore, this diagnosis is less likely.

Cryoglobulinaemia type 1 is not associated with hepatitic C. Associations include multiple myeloma and Waldenstrom macroglobulinaemia.

Cryoglobulinaemia type 3 is not associated with hepatitic C. Associations include rheumatoid arthritis and Sjogren's.

Warm autoimmune haemolytic anaemia is the most common form of autoimmune anaemia. It is idiopathic in 50% of cases. In others, it is often associated with another autoimmune disease such as rheumatoid arthritis or systemic lupus erythematosus. Therefore, this diagnosis is unlikely in this case.

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A 40-year-old man presents to the Emergency Department with non-specific symptoms of lethargy, malaise, headache, body aches, a low-grade fever and a sore throat. The examination is essentially normal aside from multiple limb petechiae. Tympanic temperature is 37.6°C. Blood pressure, heart rate and pulse oximetry are normal.

Blood tests show:

Haemoglobin	112g/L	Sodium	136mmol/L
MCV	82fL	Potassium	4.5mmol/L
Platelets	77x10^9/L	Urea	6.9mmol/L
White cells	32x10^9/L	Creatinine	111µmol/L
Prothrombin time	23secs	CRP	54mg/L
Fibrinogen	0.45g/L	HIV test	Negative
Liver enzymes	normal		

The automated counter is unable to supply differential white cell count.

Manual blood film shows immature granulocytes with bilobed nuclei and Auer rods.

What is the most important immediate therapy to institute?

A. All trans retinoic acid (ATRA) [tretinoin]
B. Methotrexate
C. Imatinib
D. Rituximab
E. Arsenic trioxide

A. All trans retinoic acid (ATRA) [tretinoin]

APML is treated with all-trans retinoic acid (ATRA) to force immature granulocytes into maturation to resolve a blast crisis prior to more definitive chemotherapy

The above vignette gives a classical description of acute promyelocytic leukaemia (APML). This diagnosis is considered a haematological emergency. Approximately 10% of patients with an acute leukaemia are ultimately diagnosed with APML but it is a largely unconsidered diagnosis. If diagnosed, it is one of the most treatable leukaemias, however, in one-third of cases the initial presentation is of catastrophic haemorrhage.

The average age of presentation with APML is 30-40 which distinguishes it from other acute myeloid leukaemias which present in the seventh decade typically. Other presenting symptoms are similar however with fatigue and weakness due to anaemia, coryzal or influenza symptoms and easy bruising due to thrombocytopaenia and coagulopathy. Myeloid leukaemia may cause splenomegaly which is usually absent in APML. Lymphadenopathy does not occur in leukaemias of myeloid line.

A blood film may show characteristic Auer rods in both myeloid leukaemia and APML. The film will show abnormal myeloid precursor cells or granulocytes in APML which are often bilobar or multilobar, whereas leukaemic mature myeloid cells are present in other forms of myeloid leukaemia although distinguishing these is difficult. Automated counters may fail to determine a differential white cell count. Confirmation of AMPL is via polymerase chain reaction or fluorescent in-situ hybridisation (FISH) of the bone marrow which demonstrates translocation of chromosomes 15 and 17. A gene on chromosome 17 codes for the retinoic acid receptor alpha protein and in APML patients with this translocation, administration of all-trans retinoic acid forces the immature myeloid cell to mature and it then undergoes apoptosis. ATRA is considered an emergency treatment for an APML blast crisis in those with coagulopathy or severe anaemia or sepsis. ATRA is considered only an emergency drug to force cell maturation; ongoing chemotherapy is required to maintain remission. Current guidelines recommend arsenic trioxide as the first line agent to achieve remission once ATRA therapy is commenced and also in refractory disease.

Methotrexate may sometimes be used to maintain remission in some APML patients although it is not helpful in the acute presentation.

Imatinib is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukaemia, particularly those with the Philadelphia translocation. It is not commonly used in this scenario.

Rituximab is a monoclonal antibody against CD20 on B cells. It has many uses in inflammatory diseases, lymphoma and lymphocytic leukaemia but is rarely used in APML or myeloid leukaemia (since B cells are of lymphoid, not myeloid lineage). There are some studies which have suggested a link between rituximab usage and the development of APML.

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A 43-year-old man presents to the emergency department with melaena and haematemesis. He has a past medical history of immune thrombocytopenia and is not currently on any treatment. He does not drink alcohol.

Observations:

Heart rate 108 beats per minute Blood pressure 92/58 mmHg Respiratory rate 18/minute Oxygen saturations 96% on room air Temperature 37.1ºC

On examination, there is dried blood around the patient's mouth. Ecchymoses are noted on his arms and abdomen. There is melaena per rectum. There are no signs of chronic liver disease.

Blood tests:

Hb	73 g/L	Male: (135-180)Female: (115 - 160)
Platelets	9 * 10 /L	(150 - 400)
WBC	8.2 * 10 /L	(4.0 - 11.0)
Na	137 mmol/L	(135 - 145)
K	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	89 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	12 µmol/L	(3 - 17)
ALP	38 u/L	(30 - 100)
ALT	27 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	38 g/L	(35 - 50)
Prothrombin time	11 seconds	(10-12)

Given the clinical history, what is the most appropriate choice of treatment to raise the platelet count?

A. Azathioprine
B. Intravenous immunoglobulin
C. Prednisolone
D. Rituximab
E. Romiplostin

B. Intravenous immunoglobulin

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

Intravenous immunoglobulin (IVIG) is correct. The patient presents with life-threatening bleeding and a platelet count of 9. The fastest way to increment the platelet count in ITP is with IVIG, which is indicated in cases of life-threatening bleeding. The expected response time is 1-3 days. In cases of life-threatening bleeding, platelets are typically given in addition.

Prednisolone is incorrect. This is the typical first-line treatment for ITP. However, in cases of lifethreatening bleeding and where the platelet count needs to be incremented quickly, IVIG is more effective. The expected response time is 4-14 days.

Rituximab is incorrect. This is used in refractory cases and takes between 7-56 days to raise the platelet count. It would not be used in the first instance.

Azathioprine is incorrect. This can be used as a steroid-sparing agent in ITP but it takes between 30-90 days to work and would therefore not be used in an emergency such as this case.

Romiplostim is incorrect. This is a fusion protein that activates the thrombopoietin (TPO) receptor and increases platelet production. It takes between 5-14 days to raise the platelet count

Question 19 of 191

A 36-year-old female was referred to the outpatient haematology clinic having been referred by her GP with a falling white cell count. Eight weeks ago she saw her own GP complaining of feeling continuously tired after a viral upper respiratory illness two weeks prior to the onset of her symptoms. She also complained of feeling generally unwell and of having intermittent pains in all her joints and muscles without swelling or stiffness. Her respiratory symptoms had fully resolved and she denied any night sweats or weight loss. Her GP organised a set of screening blood investigations which revealed a white cell count of 2.6 *10^9 g/dl (neutrophil count 2.0 *10^9 g/dl). This was repeated on two further occasions over the next four weeks revealing results of 2.2 and 1.9 respectively (neutrophil counts of 1.5 *10^9 g/dl and 1.2 *10^9 g/dl respectively). Her past medical history included hypothyroidism for which she was treated with levothyroxine 150mcg OD.

Examination at the clinic revealed the presence of a systemically well female. Her blood pressure was 118/74 mmHg, heart rate 82 bpm, respiratory rate 16/min and temperature 36.6ºC. Examination of her cardiovascular system was unremarkable. Similarly, examination of her gastrointestinal system was unremarkable, with no organomegaly identified. No cervical, axillary or inguinal lymph nodes were palpable. Examination of her ENT system was unremarkable.

Initial investigations at the clinic revealed the following results:

Hb	122 g/l
WCC	2.0 * 10 /l
Neutrophils	1.3 * 10 /l
Lymphocytes	0.6 * 10 /l
Monocytes	0.1 * 10 /l
Platelets	224 * 10 /l
Blood film	Neutropaenia
B12	224 (NR 160-900 ng/l)
ESR	15 mm/hr
CRP	9 mg/l
TSH	0.35 (NR 0.4-3.6mu/ml)
FT4	11.6 (NR 4.5-13.6 mcg/dl)
Monospot test	Negative
CMV serology	Negative

What is the single most appropriate management option?

A. Organise bone marrow aspirate and biopsy
B. Organise peripheral blood flow cytometry analysis
C. Repeat full blood count in four weeks
D. Organise CT neck, thorax, abdomen and pelvis
E. Organise blood cytogenetic analysis

C. Repeat full blood count in four weekssss

This is a very common scenario seen in the haematology outpatient clinic. This patient most probably has transient myelosuppression secondary to a viral infection with post viral fatigue and malaise. Although she is symptomatic, she is systemically well and there are no other red flag symptoms or signs including the presence of lymphadenopathy and splenomegaly. Her neutrophil count has been falling but it has remained above 1 and she is not febrile or septic. Her neutrophil count is beginning to improve (albeit very slowly) and therefore a repeat FBC would be justified to ensure that it does return to normal. If it remains low further investigation would be justified.

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You are asked to review a 74-year-old man on the haematology ward. He complains of widespread bruising and bleeding gums. He has a past medical history of myelodysplasia. He has required 6 red cell transfusion and 5 platelet transfusions in the past 12 months.

Blood results are as follows:

Hb	95 g/l
Platelets	8 * 10 /l9
WBC	4.2 * 10 /l9

You decide to transfuse him 1 unit of platelets. A repeat blood test the following day is reported below:

Hb	92 g/l
Platelets	12 * 10 /l9
WBC	3.8 * 10 /l9

What investigation will you order next?

A. Anti HLA antibodies
B. Platelet Factor 4 Antibody
C. Von Willebrand factor (vWF) levels
D. Lupus anticoagulant
E. Anti-β2 glycoprotein

A. Anti HLA antibodies

HLA-matched platelets and single-donor platelets are used for individuals that are refractory to platelet transfusions and have developed anti-HLA or antiplatelet antibodies

Platelet refractoriness is a failure to obtain a satisfactory response to a platelet transfusion on two or more occasions. An unsatisfactory response is defined by a platelet rise of less than 10 * 10 /l. When a patient does not have a satisfactory response to a platelet transfusion it is important to establish exactly why this has occurred. There are many mechanisms which can play a role including both immunological (e.g. alloimmunisation) and non-immunological (e.g. splenomegaly, DIC and sepsis).

This patient has had multiple previous platelet transfusions, making alloimmunisation high up in the differential. It is therefore important to check for anti-HLA or antiplatelet antibodies. HLAmatched platelets and single-donor platelets are used for individuals that are refractory to platelet transfusions and have developed anti-HLA or antiplatelet antibodies.

Platelet Factor 4 (PF4) antibodies are checked when heparin induced thrombocytopenia is suspected.

Anti-β2 glycoprotein and lupus anticoagulant are checked when antiphospholipid syndrome is suspected.

Question 21 of 191

The hospital is running low on its stock of cytomegalovirus (CMV) seronegative blood products. All the blood products are routinely leuko-depleted to reduce the risk of transferring CMV. You are asked to prioritise patients for CMV seronegative blood.

From the following options, which patient is the highest priority?

A. Patient having post-partum haemorrhage after delivery of twins
B. Patient on high dose oral steroids for temporal arteritis
C. Patient with HIV with CD4 count 50, not on anti-retroviral therapy
D. Patient with acute myeloid leukaemia who is planned for haematopoietic stem celltransplant next week
E. Patient with previous CMV pneumonitis

D. Patient with acute myeloid leukaemia who is planned for haematopoietic stem celltransplant next week

The use of CMV-seronegative blood products is reserved for CMV-seronegative individuals that are likely to proceed to haematopoietic stem cell transplant, or neonates

The correct answer is patient 4 who is planning for a haematopoietic stem cell transplant. The patient with the post-partum haemorrhage and the patient with severe anaemia secondary to upper GI bleed both require emergency transfusion but do not require CMV negative blood.

Other patients that should receive CMV-negative blood are neonates and pregnant women (other than during delivery). Blood from a patient who is seropositive for CMV is potentially infectious to the recipient due to either infectious virus in the plasma or latent virus in the monocytes in the blood. Blood products are leuko-depleted to remove the white blood cells to reduce the risk of transmission via monocytes. The use of seronegative blood has a lower risk of transfer to CMV but there is still a possible risk of transmission, as the antibodies take time to become positive after the donor has been infected.

Post-partum haemorrhage: pregnant women should be given seronegative blood if possible during pregnancy to prevent CMV infection of the fetus. This does not apply during or after delivery because there is no risk to the fetus, so this patient would not require seronegative blood.

High-dose oral steroids: this patient does not require seronegative blood because immune suppression is not an indication for seronegative blood products.

HIV infection is not an indication for seronegative blood products even in advanced untreated disease.

Previous CMV pneumonitis: this patient has already been infected with CMV and therefore does not require seronegative blood products.

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A 23-year-old man presents with diffuse bruising, abdominal pain, and loss of appetite. He feels unwell and has no history of taking any medications, does not use dietary supplements, and does not use illicit drugs. His past medical history is negative for any prior illnesses or hospitalisations. No family history of any bleeding disorders.

On examination, he has a heart rate of 115 bpm with a blood pressure of 130/75mmHg. His respiratory rate is 18 breaths per minute and he is afebrile with a temperature of 37.2ºC. His abdominal exam demonstrates rebound tenderness in the right lower quadrant.

Investigations:

Hb	13.7 g/L	(135-180)
Platelets	48 * 10 /L 9	(150 - 400)
WBC	5 * 10 /L 9	(4.0 - 11.0)
Haematocrit	41%	(41-50%)
INR	1.1	(0.9-1.2)
Fibrinogen	2.2 g/L	(2 - 4)

A diagnosis of acute appendicitis is made and the general surgical team decides that the patient needs to be taken to theatre for an urgent laparoscopic appendectomy.

What is the next best step in his management?

A. Antithymocyte globulin plus ciclosporin
B. Give intravenous glucocorticoid
C. Haematopoietic stem cell transplant
D. Start intravenous human immunoglobulin
E. Urgent platelet transfusion

D. Start intravenous human immunoglobulin

Human immunoglobulin (IVIG) is an alternative to steroids in treating ITP, particularly if the platelets need to be raised quickly

Primary immune thrombocytopenia (ITP, also called idiopathic thrombocytopenic purpura, immune thrombocytopenic purpura) is acquired thrombocytopenia caused by autoantibodies against platelet antigens leading to platelet destruction and platelet underproduction that is not triggered by an apparent associated condition. The likely diagnosis is ITP here as the patient has normal white cell counts and haemoglobin, no other causes of coagulopathy with normal PT/INR, no family history of bleeding disorder and clinically no organomegaly.

IVIG can raise the platelet count within 12 to 24 hours in many patients with ITP; this effect is reproducible enough that a platelet count response to IVIG has been used as a diagnostic criterion for ITP. The effect of IVIG usually persists for two to six weeks. Thus, IVIG is most useful for patients who require a rapid, temporary increase in platelet count (for urgent management of bleeding associated with thrombocytopenia or before an urgent invasive procedure) or those who are unable to tolerate glucocorticoids and are awaiting initiation of second-line therapy.

IV glucocorticoid therapy is incorrect as it's not preferred therapy in this situation where there is a need for urgent surgery. IVIG may be used either as an adjunct to other therapies in an individual with critical bleeding or need for urgent surgery or as an alternative to glucocorticoids in patients with severe bleeding.

Urgent platelet transfusion will be an ineffective treatment in immune (idiopathic) thrombocytopenic purpura especially when planning for immediate surgery as it is controversial, as transfused platelets are short-lived and platelet transfusion has been linked to arterial thrombosis and mortality in platelet consumptive disorders like ITP.

Antithymocyte globulin plus ciclosporin is not the right option for treatment here as it is used in immune-mediated aplastic anaemia.

Haematopoietic stem cell transplant is not applicable in this situation as it is the best treatment for young patients with aplastic anaemia with the best match available.

Question 23 of 191

A 56-year-old woman presents with lethargy and vomiting to her GP. She is normally fit and well. Blood tests and a urine sample are sent.

Hb	110 g/L /L 9	Female: (115 - 160)
Platelets	160 * 10 /L 9	(150 - 400)
WBC	5 * 10 /L 9	(4.0 - 11.0)
Na +	132 mmol/L	(135 - 145)
K +	4.8 mmol/L	(3.5 - 5.0)
Urea	11.1 mmol/L	(2.0 - 7.0)
Creatinine	140 µmol/L	(55 - 120)
Calcium	3.0 mmol/L	(2.1-2.6)
Phosphate	1.2 mmol/L	(0.8-1.4)
Magnesium	0.8 mmol/L	(0.7-1.0)

Urine electrophoresis is positive for Bence Jones protein.

Given the likely underlying diagnosis, what imaging is recommended to assess for bony involvement?

A. DEXA scan
B. Isotope bone scan
C. No imaging required at diagnosis
D. Whole body MRI
E. X-rays of spine and pelvis

D. Whole body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

The presence of hypercalcaemia, acute kidney injury and Bence Jones proteins in the urine is highly suggestive of a diagnosis of multiple myeloma. In their 2016 guidelines, NICE recommends whole-body imaging at diagnosis of multiple myeloma to assess for bony involvement. They recommend whole-body MRI as first line. Whole-body CT or positron emission tomography (PET) scans can be used as alternatives if MRI is inappropriate or unavailable. The other options are not recommended as first-line imaging modalities in this circumstance by NICE.

A DEXA scan is used in combination with a FRAX tool assessment to assess for future fracture risk in patients with known or suspected osteoporosis.

Nuclear medicine scans such as an isotope bone scan are not recommended as first-line imaging in this situation. Some indications for isotope bone scans include investigating for Paget's disease, osteomyelitis or in primary bone malignancies.

In their 2016 guidelines, NICE recommends whole-body imaging at the time of diagnosis of myeloma to assess for bony involvement.

X-rays can show typical lytic lesions associated with bony involvement in myeloma. However, Xrays are inadequate to exclude bony involvement and are therefore not recommended as first-line imaging in this circumstance.

Question 24 of 191

A 43-year-old man with acute pancreatitis is being treated in the surgical ward. Whilst an inpatient, he experiences recurrent epistaxis, gingival bleeding, and haematuria.

He is re-examined and multiple petechiae are noted as well as some mild confusion. He is somewhat hypotensive when observations are recorded.

Blood tests are taken:

Platelets	83 * 10 /L 9	(150 - 400)
Prothrombin time (PT)	26 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	48 secs	(25-35 secs)
Fibrinogen	0.3 g/L	(2 - 4)

As well as general resuscitation, what else is most useful, first-line?

A. Cryoprecipitate
B. Fibrinogen concentrate
C. Fresh frozen plasma
D. Platelet transfusion
E. Tranexamic acid

C. Fresh frozen plasma

In bleeding patients with DIC and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), administration of fresh frozen plasma (FFP) may be useful

This patient has developed disseminated intravascular coagulation (DIC), a syndrome characterised by coagulation pathway activation, leading to intravascular thrombi and depletion of platelets and coagulation factors. It is triggered by an underlying condition - in this scenario, acute pancreatitis. As well as treatment of the underlying disorder, the most useful additional option here is **fresh frozen plasma**. This is the preferred method of replacing coagulation factors when bleeding is present or when fibrinogen levels are low.

Cryoprecipitate is a second-line alternative. Fresh frozen plasma is still preferred with regards to DIC.

Similarly, **fibrinogen concentrate** may be used as second-line alternatives. However, fresh frozen plasma is the first-line choice for DIC.

Platelet transfusion is generally considered when the platelet count is less than 20 * 10 /L, or less than 50 * 10 /L in the presence of active bleeding. In this scenario, therefore, this is not as important a consideration as the administration of fresh frozen plasma.

Tranexamic acid may be used in the management of chronic DIC, under specialist guidance. It should be used with extreme caution as it inhibits fibrinolytic pathways, which may worsen thrombosis. In the acute setting, such as this scenario, it does not play a role.

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A 23-year-old man presents to the emergency department acutely unwell for the last 72 hours. He has been fatigued for the last month and has been having night sweats and has had several colds. Over the last 3 days, he has become more unwell, shivery and vomiting. He has noticed bruising on forearms and thighs. On examination, he is drowsy and has a temperature of 38.5ºC. His blood pressure is 90/50 mmHg, heart rate 120/min. He is peripherally shut down with a cap refill time of 5 seconds. He has conjunctival pallor. He is given IV fluids and antibiotics by the emergency department. His blood results show:

Hb	89 g/l
Platelets	43 * 10 /l
WBC	13.0 * 10 /l
Neutrophils	9.0 * 10 /l
D-Dimer	5.8mg/L (<0.5)
INR	8.5
PT	89 seconds (9-12)
APTT ratio	1.7 (0.8-1.2)
Fibrinogen	0.1g/L (1.5 - 4.5)
Blood film	Faggot cells seen
Na	138 mmol/l
K	5.8 mmol/l
Urea	18 mmol/l
Creatinine	195 µmol/l
CRP	170 mg/l
Bilirubin	8 µmol/l
ALP	102 u/l
ALT	300 u/l
Albumin	38 g/l

He is transferred to ITU for ionotropic support. He is treated with fresh frozen plasma which corrects his coagulopathy. Haematology is involved and he has a bone marrow analysis performed. Cytogenetics shows a translocation of chromosomes 15 and 17. ***What is the appropriate treatment to give***?

A. All-trans retinoic acid
B. R-CHOP
C. Chlorambucil
D. High dose prednisolone
E. Ribavirin

A. All-trans retinoic acid

This patient has acute promyelocytic leukaemia (M3 subclass). This can present with DIC in young patients the prolonged prothrombin time, with platelets consumption and low fibrinogen. Faggot cells are hypergranular promyelocytes, so called because the high concentrations of Auer rods in the cytoplasm give the cells a bundle of sticks appearance. The gene translocation of 15:17 results in a fusion gene of PML:RARa (retinoic acid receptor). The exact process by which this gene fusion results in AML is unclear but the condition responds well to retinoic acid therapy hence this is the correct answer here. The other options are for other types of haematological malignancy.

Question 26 of 191

A 37-year-old woman was admitted to the Intensive Care Unit (ICU) two days following chemotherapy. She had received her third of six cycles of chemotherapy for malignant ovarian cancer and without initial complication and was discharged the same day. Two days later she felt unwell and developed a fever. After liaising with the oncology unit she was admitted directly to the Medical Admission Unit. A full septic screen was conducted and she was treated empirically for neutropaenic sepsis with intravenous tazocin and gentamicin. Other than malignant ovarian cancer her past medical history was unremarkable, and there was no known metastasis. She was not taking any other drug therapy and was a non smoker. She did not consume alcohol.

Unfortunately whilst on the Medical Admission Unit she continued to deteriorate, developing fluctuating hemiparesis of initially the left lower limb, and then the right upper limb. Her level of consciousness dropped and her speech had become slurred. An urgent transoesophageal echocardiogram and CT head scan was conducted, pending availability of a MRI scan. She was promptly transferred to the Intensive Care Unit.

Upon arrival at the ICU she appeared very unwell, with a GCS of 12/15. Her blood pressure was 188/96 mmHg, her heart rate was 112, her respiratory rate was 22/min and her temperature was 38.5 degrees celsius. Examination of the cardiovascular system revealed the presence of normal heart sounds, a JVP of 3cm and warm well perfused peripheries. Examination of the respiratory system revealed good air entry in both lungs, with an oxygen saturation of 95% on air. Examination of her gastrointestinal system was unremarkable. Examination of her neurological system revealed localization to pain stimulus, with confusion and eye opening only in response to verbal prompting. Her speech was slurred. There was no other apparent focal neurological deficit, with otherwise normal cranial nerve and peripheral nervous system testing.

The results of the investigations conducted are as follows:

Hb	89g/l
Platelets	38 * 10 /l
WBC	15.2 * 10 /l
Reticulocyte count	4% (ie above normal range)
Blood film	presence of schistocytes, normocytic normochromic anaemia
Na	136 mmol/l
K	6.1 mmol/l
Urea	10.1 mmol/l
Creatinine	154 µmol/l
CRP	22 mg/l
ESR	45 mm/hr
Protein	78 g/l
Albumin	36 g/l
Adj calcium	2.42 mmol/l
Phosphate	0.95 mmol/l
Bilirubin	44 µmol/l
ALT	39 u/l
LDH	1286 u/l
ALP	102 u/l
PTT	14s
APTT	44s
INR	1.1
D-dimer	136 ng/ml

Chest x-ray: normal heart and lung appearances

ECG: heart rate 107bpm normal sinus rhythm, normal QRS and QTc intervals Urinalysis: proteinuria ++, haematuria +, leuc/nit/glu negative

Blood MCS x3: pending result Urine MCS: pending result

CT head: no space occupying lesion, mass shift or intracerebral haemorrhage seen Transoesophageal echocardiogram: normal systolic function, normal appearance of all valves, no evidence of vegetation seen

In the context of the likely underlying diagnosis, what is the best immediate management step?

A. Commence immediate plasma exchange
B. Commence high dose intravenous hydrocortisone
C. Commence platelet infusion
D. Commence IV meropenem and IV antifungal therapy
E. Commence fresh frozen plasma infusion

A. Commence immediate plasma exchange

This patient has developed thrombotic thrombocytopaenia purpura (TTP) secondary to chemotherapy, as manifested by the combination haemolytic anaemia, thrombocytopaenia and acute renal impairment. The presence of a fever and neurological involvement differentiates this condition from haemolytic-uraemic syndrome. Of the above options, plasma exchange holds the best prognosis for this condition and is, therefore, the best option to be initiated without delay, but in practice glucocorticoids and fresh frozen plasma infusions are often given pending arranging plasma exchange.

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A 22-year-old man with sickle cell disease is seen in the Emergency Department. He has had worsening pain in his arms and legs for the last 2 days and 5 hours ago developed a painful sustained erection.

He has felt otherwise well recently and has no other past medical history. He is on regular paracetamol, ibuprofen, folate and penicillin. He does not receive regular transfusions and has been admitted with a crisis only once before. He has never had an episode of painful sustained erection.

On examination he has a heart rate of 110 beats per minute and a blood pressure of 132/95 mmHg. His oxygen saturations are 96% on room air and he is afebrile. His chest is clear and abdomen is soft. He has no swelling or erythema of his limbs, though they are generally tender. He continues to have an erection, though there is no sign of ischaemia.

His chest x-ray shows clear lung fields. His blood tests are as follows:

Hb	78 g/l	Na +	141 mmol/l
Platelets	331 * 10 /l 9	K +	3.7 mmol/l
WBC	9 * 10 /l 9	Urea	5 mmol/l
Neuts	7 * 10 /l 9	Creatinine	86 µmol/l
Lymphs	1.6 * 10 /l 9	CRP	14 mg/l

He is treated with intravenous fluids and generous analgesia with diamorphine. His limb pain is improved but he continues to have a painful erection.

What is the next most appropriate step

A. Adrenalin
B. Diethylstilbestrol
C. Exchange transfusion
D. Review by urologist
E. Sildenafil

D. Review by urologist

This gentleman has priapism, a sustained painful erection lasting 4 hours. If left untreated it can result in impotence. Current guidelines recommend initial conservative management with fluids and analgesia. Although any interventions beyond this have variable results, evidence supports prompt urology review to determine the need for surgical management including drainage. There is insufficient evidence to recommend routine exchange transfusions. Sildenafil, diethylstilbestrol and adrenalin may be used in consultation with urology but evidence of benefit is variable.

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A 23 year old male of Nigerian descent is referred from the ED with acute shortness of breath associated with fever and dry cough. His shortness of breath has limited him to an exercise tolerance of around 10 yards. He also complains of excruciating right sided chest pain. He is known to have sickle cell anaemia and has had no admissions to the hospital in the last 3 years.

Observations

- heart rate 94bpm regular
- blood pressure 112/74 mmHg
- temperature 38.3
- respiratory rate 22
- urine output under 30ml/hr oxygen saturations 93% on room air

Examination

respiratory system shallow breathing, bronchial breath sounds with crepitations to right base

Blood results:

Hb	7.7 g/dl
Platelets	200 * 10 /l9
WBC	13.2 * 10 /l9
Bilirubin	36 µmol/l
Urea	8.2 mmol/l
Creatinine	146 µmol/l

What is the most important initial steps in management?

A. Oxygen, IV fluids, antibiotics and analgesia
B. 2 unit blood transfusion and analgesia
C. Oxygen and analgesia only
D. Antibiotics and IV fluid only
E. Plasmapheresis and analgesia

A. Oxygen, IV fluids, antibiotics and analgesia

It is important to recognise and treat sickle cell crises (as detailed above) as a matter of urgency. This condition can be quickly fatal. This patient should be treated as per sepsis guidelines. It is crucial to adequately control the pain in this patient cohort as not being able to inhale deeply due to pain will only serve to worsen the lung damage. Early assessment for the involvement of the critical care

team is required as acute respiratory distress syndrome is a real possibility. Oxygen saturation levels should be maintained above 95% in a patient where a normal steady state level is not known. Management of this and the haemaglobin level should be specific for the patient and compared to past levels. The question states that the patient has had no admissions to the hospital in the last 3 years and as such the aim should be to keep oxygen saturations above 95%.

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A 64-year-old female undergoing chemotherapy treatment with mitomycin for bladder cancer presents to the Emergency Department with confusion, epistaxis and a widespread rash. On examination, she is febrile and has a diffuse petechial rash.

Hb	10.6g/dl
Platelets	54 * 10 /l9
WBC	11.2 * 10 /l9
Urea	11mmol/l
Creatinine	117µmol/l
Bilirubin	58µmol/l
ALP	42u/l

A blood film shows fragmented erythrocytes.

What is the most appropriate treatment for this patient?

A. Renal dialysis
B. Supportive treatment
C. A pool of platelets and fluid resuscitation
D. Urgent plasma exchange
E. IV tazocin, a pool of platelets and fluid resuscitation

D. Urgent plasma exchange

Thrombotic thrombocytopenic purpura (TTP) is characterised by fluctuating neurological signs, fever, renal dysfunction, microangiopathic haemolysis and thrombocytopenia. The key to diagnosis is differentiating between TTP and haemolytic-uraemic syndrome (HUS). The presence of neurological signs in TTP and more severe renal dysfunction in HUS usually helps in distinguishing the two.

Congenital TTP is caused by a deficiency in von Willebrand factor. However, the majority of cases are secondary and can occur in pregnancy, HIV and associated with some drugs. In particular, the chemotherapeutic agents mitomycin C, bleomycin, tamoxifen and gemcitabine are all associated with secondary TTP. Other drugs in association include penicillin, rifampicin and mmunosuppressive drugs eg. ciclosporin A.

The standard treatment for TTP is IV plasma exchange which should be initiated as soon as possible.

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A 22-year-old man attends the emergency department with a group of friends from a university party. He complains of worsening shortness of breath and light-headedness. He appears panicked and is clutching his chest. There is no past medical history of note and he has no allergies.

His observations are as follows:

- Temperature 36.2ºC
- Heart rate 112 beats/min
- Blood pressure 120/75mmHg
- Respiratory rate 24 breaths/min
- Oxygen saturations 90% on air

On examination, his lips are cyanosed. His chest is clear with good air entry bilaterally and his heart sounds are normal. Peripheral pulses are present with a capillary refill of <2 seconds and his calves are soft and non-tender.

Arterial blood gas:

pH	7.21	(7.35 - 7.45)
pO 2	12.1 kPa	(11 - 14.4)
pCO 2	2.4 kPa	(4.6 - 6.4)
Bicarbonate	16 mmol/L	(22 - 29)
Chloride	100 mmol/L	(95 - 108)
Lactate	1.2 mmol/L	(0.5 -2.2)
Glucose	5.6 mmol/L	(4 - 7)

Given the likely diagnosis, which of the following is the most appropriate next step in the management of this patient?

A. Fomepizole
B. Hyperbaric oxygen
C. Methylene blue
D. Thrombolysis
E. Intravenous 1.26% sodium bicarbonate

C. Methylene blue

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe3+ (ferric) to Fe2+ (ferrous)

This patient has methaemoglobinaemia, likely secondary to drug misuse (e.g. amyl nitrite poppers) at a party. In patients with methaemoglobinaemia, haemoglobin has been oxidised from Fe^{2+} to Fe^{3+}. This oxidised form of haemoglobin cannot bind to oxygen and therefore symptoms include cyanosis, shortness of breath and headache. In more severe illnesses, investigations may detect metabolic acidosis and arrhythmias. During methaemoglobinaemia, a normal PO may be seen with reduced oxygen saturations, similar to this patient. The treatment of choice for methaemoglobinaemia is intravenous methylene blue, which causes a reduction reaction to convert Fe^{3+} back to Fe^{2}.

Fomepizole is used in the treatment of ethanol toxicity. Symptoms of ethanol toxicity are initially similar to alcohol excess with confusion, slurred speech and altered gait. Metabolic acidosis and acute kidney injury follow. However, ethanol toxicity does not explain this patient's hypoxia and cyanosis and is less likely to be correct.

Hyperbaric oxygen therapy is used in the treatment of carbon monoxide poisoning. Unlike methaemoglobinaemia, symptoms of carbon monoxide poisoning include headache, confusion and nausea and vomiting. Respiratory symptoms are less predominant compared to methaemoglobinaemia. Carbon monoxide poisoning tends to produce a normal oxygen saturation level with a low PO , unlike this patient. It also does not explain this patient's metabolic acidosis and suggests an alternative diagnosis.

Thrombolysis would be an option for the treatment of a thrombotic cause of this patient's symptoms (e.g. pulmonary embolism). However, patients with a pulmonary embolism are more likely to

have a metabolic alkalosis secondary to hyperventilation, in contrast to this patient with metabolic acidosis.

Sodium bicarbonate can be used to treat severe metabolic acidosis. However, it is not used firstline in the treatment of methaemoglobinaemia and the priority should be to reverse the oxidation process of haemoglobin..

Question 31 of 191

A 33-year-old patient presents to the emergency department feeling very lethargic and tired over the last week. He has been increasingly short of breath on exertion and his exercise tolerance has fallen to a few hundred yards before he is out of breath. He is a known sickle cell disease patient who is managed by the Haematology team in your hospital. On examination he is afebrile and heart rate and blood pressure are within normal limits. His respiratory rate is 16/min and his oxygen saturation is 98% on air. He does become noticeably short of breath on minimal movement.

His blood tests show:

Hb	65 g/l
Platelets	46 * 10 /l
WBC	2.5 * 10 /l
Neuts	1.2 * 10 /l
Haptoglobins	1.9 g/L (0.3-2.0)
Reticulocytes	8.9 x10^9/L (25-80)
Na	136 mmol/l
K	3.9 mmol/l
Urea	7.4 mmol/l
Creatinine	78 µmol/l
CRP	<3 mg/L(<10)
LDH	200 IU/L (200-500)
Bilirubin	4 µmol/l
ALP	89 u/l
ALT	34 u/l
Albumin	39 g/l

His chest x-ray is normal.

On further questioning, he tells you that his 5-year-old daughter was unwell 3 weeks ago. He took her to see the GP and was told it was likely to be a viral illness.

What is the most likely cause for his blood results as shown?

A. Parvovirus B19
B. Acute chest crisis
C. Splenic sequestration
D. HIV
E. Legionella pneumoniae

A. Parvovirus B19

This gentleman has had an aplastic sickle cell crisis as a result of parvovirus infection. He has symptomatic anaemia. There is nothing to suggest splenic sequestration and he is too well for an acute chest syndrome. The normal chest x-ray is not in keeping with a pneumonia. HIV is a possibility but less likely given the clinical picture.

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A 79-year-old woman has been referred to the clinic due to weight loss, right-sided chest pain, lower back pain, and general fatigue.

Hb	96 g/L	Male: (135-180)Female: (115 - 160)
Platelets	399 * 10 /L 9	(150 - 400)
WBC	10.2 * 10 /L 9	(4.0 - 11.0)
Na +	145 mmol/L	(135 - 145)
K +	4.5 mmol/L	(3.5 - 5.0)
Urea	15.2 mmol/L	(2.0 - 7.0)
Creatinine	190 µmol/L	(55 - 120)
Calcium	3.1 mmol/L	(2.1-2.6)
Phosphate	1.4 mmol/L	(0.8-1.4)
Magnesium	0.7 mmol/L	(0.7-1.0)

Urine Bence Jones: positive

She is usually fit and well with no past medical history.

What would be the first-line imaging to confirm the most likely diagnosis?

A. CT thorax, abdomen, and pelvis
B. Chest radiograph
C. PET CT
D. Skeletal survey
E. Whole-body MRI

A. Whole-body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

The most likely diagnosis here is multiple myeloma given the weight loss, bone pain, anaemia, renal impairment, and hypercalcemia.

Further tests should be sent to clarify this diagnosis including serum free light chains, serum protein electrophoresis, and immunoglobulins.

It is worth noting that guidance regarding the answer to this question may vary from hospital to hospital depending on availability, but national guidance recommends whole-body MRI as firstline imaging.

Whole-body MRI is the correct answer. Part of the diagnostic criteria for multiple myeloma is the presence of 1 or more osteolytic lesions of ≥5 mm. This is most sensitively picked up on MRI scanning, which can also pick up pre-lytic lesions that may be amenable to biopsy.

CT thorax, abdomen, and pelvis is incorrect. CT scanning has a lower sensitivity for osteolytic lesions. There is also higher radiation exposure.

PET CT is incorrect. This type of scanning can be helpful for looking at intramedullary involvement, but the consensus from current best evidence is that MRI is preferable particularly to identify osteolytic lesions.

Skeletal survey is incorrect. It is less sensitive and specific compared to PET CT and MRI scanning. This is the preferred option for patients who are unable to undergo whole-body MRI, PET CT, or CT. It takes less time to perform compared to whole-body MRI (25 minutes as opposed to 60 minutes).

Chest radiograph is incorrect. Although this is a sensible first-line test to perform in the acute setting, this question asks

specifically about the first-line test for the most likely diagnosis here - multiple myeloma. Chest radiograph is therefore incorrect.

Question 33 of 191

A 23-year-old female has presented with her first episode of seizure on the labour ward, 2 days after delivering her first child by normal vaginal delivery. She reports a fluctuating generalised headache over the past 3 months but had not previously sought medical attention. In addition, she had spiked 2 fevers over 38ºC over the past 48 hours, with no dysuria, diarrhoea or vomiting, productive cough or signs of meningism. She has no past medical history, is a life-long nonsmoker and has been abstinent from alcohol for 9 months, previously drinking 4 units per week. Her seizure was witnessed and described as tonic-clonic jerking of all 4 limbs, associated with loss of consciousness, terminated after 4mg of intravenous lorazepam after 4 minutes. On examination, she appears post-ictal but responding to voice despite being sleepy. Pupils are reactive and equal. Plantars are downgoing bilaterally. Cardiovascular, abdominal and respiratory examinations are unremarkable. No skin rashes, neck stiffness or photophobia are noted.Her blood results are as follows:

Hb	75 g/l
MCV	87 fl
Platelets	23 * 10 /l9
WBC	9.2 * 10 /l9
Blood film	Schistocytes
Coombs' test	Negative
CRP	30 mg/l
Urea	12.6mmol/l
Creatinine	154 µmol/l
Bilirubin	28 µmol/l
ALP	98 u/l
ALT	28 u/l
γGT	23 u/l

A CT head with contrast demonstrated no areas of ischaemia, haemorrhage or space occupying lesion.

Which is the next most appropriate immediate management?

A. Plasma exchange
B. Intravenous 3rd generation cephalosporin antibiotics
C. Intravenous phenytoin loading
D. MRI head with contrast
E. Intravenous steroids

A. Plasma exchange

This young lady's blood tests demonstrated a normocytic anaemia associated with schistocytes (fragmented red cells) with negative Coombs' test, suggestive of mechanical destruction of red cells. In addition, thrombocytopaenia is present with renal impairment and normal liver function tests. The initial presentation is of first seizure and fluctuating headache, with two unexplained fevers. The pentad of fever, fluctuating neurological symptoms, microangiopathic haemolytic anaemia, thrombocytopaenia and renal impairment represents thrombotic thrombocytopaenic purpura-haemolytic uraemic syndrome spectrum (TTP-HUS), resulting in microvascular thrombus formation. There is little to suggest an underlying epilepsy syndrome and no indication for phenytoin loading after a single seizure without status epilepticus. While meningitis may cause headaches, a fluctuating 3-month history without meningism is unlikely.

Immediate treatment of TTP-HUS is reliant on plasma exchange without delay in order to remove the high-molecular weight von-Willebrand factor (vWF) driving platelet aggregation and replacing ADAMTS-13 protease, a cleavage enzyme of high molecular weight vWF often deficient in TTP patients, resulting in microvascular thrombi formation. High dose steroids may be appropriate in the setting of refractory disease despite plasma exchange but is an adjunct to plasma exchange, not in place of. Persistent recurrent or refractory TTP-HUS despite plasma exchange and steroids should be considered for the addition of rituximab or increased frequency of plasma exchange. TTP-HUS is a medical emergency and invariably results in death secondary to progressive renal failure if not treated immediately.

Question 34 of 191

A 22-year-old man presents to the emergency department with shortness of breath. He takes no regular medicines and denies the use of herbal, or over-the-counter medications. However, he does admit to using amyl nitrites recreationally.

Observations are as follows: heart rate 125 beats per minute, respiratory rate 24 breaths per minute, blood pressure 125/75 mmHg, temperature 37.2 ºC, and SpO2 92%. His chest is clear on auscultation.

He is started on 15L O2 via a non-rebreather mask. Blood gas analysis results are as follows:

pH	7.26	(7.35 - 7.45)
PaO2	72.4 kPa	(10.3 - 13.3 kPa)
PaCO2	2.9 kPa	(4.7 - 6 kPa)
HCO3	18 mmol/L	(22 - 28 mmol/L)
SaO2	48%	(94 - 98%)
Lactate	3.2 mmol/L	(<1.0)

What treatment is indicated?

A. Ascorbic acid
B. Dicobalt edetate
C. Hydroxocobalamin
D. Hyperbaric oxygen
E. Methylthioninium chloride

A. Methylthioninium chloride

Methylene blue can be used to treat methaemoglobinaemia. It causes a reduction of Fe3+ (ferric) to Fe2+ (ferrous)

The striking feature, in this case, is the significant discrepancy between the PaO2 and SaO2 on arterial blood gas analysis.

Given the patient is on 15L O2, the PaO2 is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. There are various formulas for predicting the expected PaO2 for any given inspired O2 concentration. The Advanced Life Support (ALS) guidelines suggest that the PaO2 for any given inspired concentration should be approximately 10 less than the inspired concentration (%). For example, in this case, 15L O2 is equivalent to approximately 80-85% so we would expect the PaO2 to be around 70 kPa.

However, it is important to note that the SaO2 (oxygen saturation of haemoglobin) is markedly low at 48% indicating impaired oxygen binding to haemoglobin. It is also important to note that the peripheral SpO2 is 92% which is clearly discrepant with the SaO2.

The two main causes of this picture are methaemoglobinaemia and carboxyhaemoglobinaemia. Because standard pulse oximeters are not capable of differentiating between different forms of bound haemoglobin, the SpO2 is usually falsely high in these conditions.

Tissue hypoxia can be a consequence of 4 main causes:

1. Hypoxaemia (low PaO2 due to poor gas exchange at the alveoli)

2. Toxic haemoglobin (low SaO2 due to methaemoglobinaemia or carboxyhaemoglobinaemia)

3. Perfusional (e.g. shock, or localised causes such as compartment syndrome or bowel

ischaemia)

4. Severe anaemia

Regardless of the cause, tissue hypoxia will result in lactic acidosis. Therefore, in patients with lactic acidosis, all the aforementioned causes should be considered. The patient in this case most certainly has lactic acidosis as a consequence of toxic haemoglobin-induced tissue hypoxia. He is acidotic with low serum bicarbonate since this acts as a buffer for lactic acid.

Methylthioninium chloride is correct. The patient has a diagnosis of acquired methaemoglobinaemia. As discussed above, the biochemical results are suggestive of toxic haemoglobin. The history of nitrate exposure favours the diagnosis of acquired methaemoglobinaemia. The treatment of choice is IV methylthioninium chloride (methylene blue).

Ascorbic acid is incorrect. This drug can be used to treat congenital methaemoglobinaemia. Although this remains within the differential diagnosis, the absence of previous episodes and the presence of a known risk factor (e.g. nitrate exposure) favours the acquired form.

Dicobalt edetate and **Hydroxocobalamin** are incorrect. These drugs can be used to treat cyanide poisoning. Cyanide binds the ferric (Fe3+) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO2 as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this clinical case to suggest that this is the case.

Hyperbaric oxygen is incorrect. This can be used to treat severe carboxyhaemoglobinaemia.

Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the history of nitrate exposure favours the diagnosis of methaemoglobinaemia.

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A 31-year-old lady presents to the emergency department with abdominal pain.

Her medical and surgical history is unremarkable other than mild depression and hay fever. Medications include paroxetine and PRN loratadine.

She complains of generalised colicky abdominal pain and has vomited once in the department.

On examination blood pressure is 155/86mmHg, heart rate is 95bpm and temperature is 37.9ºC. Digital rectal examination reveals hard stool in the rectum.

Investigations reveal:

Hb	131 g/l
Platelets	362 * 10 /l9
WBC	7.3 * 10 /l9
Na +	121 mmol/l
K +	3.3 mmol/l
Urea	6.2 mmol/l
Creatinine	87 µmol/l
Urine dipstick	protein ++, leucocytes ++

What is the most likely diagnosis?

A. Cholecystitis
B. Acute porphyria
C. Intestinal obstruction
D. Pyelonephritis
E. Systemic lupus erythematosus

B. Acute porphyria

The normal white cell count make infective diagnoses such as pyelonephritis and cholecystitis less likely. Intestinal obstruction usually presents with an empty rectum.

The history of neuropsychiatric symptoms along with hypertension and hyponatraemia are suggestive of acute porphyria.

Systemic lupus erythematosus doesn't tend to present with abdominal pain.

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A 34-year-old woman is rushed to the emergency department by her husband. Her husband says that she has been lethargic for the last 2 days and this morning has become increasingly more confused and behaving differently to normal. She has no past medical history of note. She is 16 weeks pregnant.

On examination, she is febrile with a temperature of 38.5ºC. She is tachycardic with a heart rate of 125 bpm and has a blood pressure of 115/95mmHg. On auscultation, her chest is clear with normal heart sounds. Her abdomen is soft and non-tender with a palpable uterus in keeping with 16 weeks gestation.

Investigations:

Hb	92 g/L	Male: (135-180)Female: (115 - 160)
Platelets	43 * 10 /L 9	(150 - 400)
WBC	6.3 * 10 /L 9	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	3.8 mmol/L	(3.5 - 5.0)
Urea	11.2 mmol/L	(2.0 - 7.0)
Creatinine	185 µmol/L	(55 - 120)
Bilirubin	32 µmol/L	(3 - 17)
ALP	35 u/L	(30 - 100)
ALT	85 u/L	(3 - 40)
Albumin	37 g/L	(35 - 50)
CRP	< 1 mg/L	(< 5)

Urinalysis: negative.

Pregnancy test: positive. What is the next immediate treatment for this patient?

A. Intravenous antibiotics
B. Intravenous immunoglobulin
C. Magnesium sulphate
D. Plasma exchange
E. Platelet transfusion

D. Plasma exchange

TTP - plasma exchange is first-line

The pentad of symptoms: AKI, fever, cerebral dysfunction, thrombocytopenia and microangiopathic haemolytic anaemia should point towards a diagnosis of thrombotic thrombocytopenic purpura (TTP). TTP is a serious condition that causes dysregulation of the clotting cascade. The underlying mechanism is not completely understood but a deficiency in the enzyme ADAMTS13 has been identified. If left untreated, TTP has a high mortality. Pregnancy is a known cause of TTP although it does not have to be present to make the diagnosis. If TTP is suspected, the first-line treatment of choice is plasma exchange. Plasma exchange removes any antibodies which inhibit ADAMTS13 whilst also replacing the functioning version of the enzyme. Steroids and rituximab have also been used to suppress the patient's immune system from producing enzymes to ADAMTS13.

Intravenous antibiotics are an appropriate consideration, given that this patient is febrile. In the absence of raised inflammatory markers, it seems more likely that fever is a symptom of TTP rather than an underlying infection. Nevertheless, even if given, antibiotic administration will not treat TTP.

Intravenous immunoglobulin is used in the treatment of refractory TTP. However, it is not the firstline treatment of choice.

Magnesium sulphate is used in the treatment of eclampsia. It is not used in the treatment of TTP.

Platelet transfusion is not recommended in TTP. Transfusion is associated with an increased risk of thrombosis and mortality.

Question 37 of 191

A 28-year-old man is admitted to the Medical Admissions Unit with a 2-day history of itching, right upper quadrant pain, and abdominal distension. The pain started as a dull ache but became constant and severe over the course of several hours.

His past medical history is remarkable only for a left lower limb DVT diagnosed at age 20. He takes no regular medications and he is a non-smoker. He drinks 2-3 units of alcohol per week and denies intravenous drug use.

Examination reveals a jaundiced young man with pale conjunctivae. He appears deeply uncomfortable. His abdomen is moderately distended with marked right upper quadrant tenderness. His liver and spleen are both palpable 2cm below the costal margin. Shifting dullness is demonstrable on percussion of the abdomen.

His blood results are as follows:

Hb	101 g/l	Na +	139 mmol/l	Bilirubin	109 µmol/l
MCV	102.4 fl	K +	4.2 mmol/l	ALP	284 u/l
Platelets	63 * 10 /l 9	Urea	6.7 mmol/l	ALT	684 u/l
WBC	12.9 * 10 /l 9	Creatinine	108 µmol/l	γGT	179 u/l
Neuts	10.8 * 10 /l 9	Albumin	27 g/l		
Lymphs	0.9 * 10 /l 9	LDH	759 u/l		

His abdominal ultrasound scan is consistent with hepatic vein thrombosis and the patient is started on low molecular weight heparin. Following a review by the Haematologists, a diagnosis of paroxysmal nocturnal haemoglobinuria is made and the patient is advised to start treatment with eculizumab.

Given the proposed treatment strategy, which of the following vaccinations should the patient be offered?

A. Hepatitis B
B. Neisseria meningitidis
C. Varicella zoster virus
D. Streptococcus pneumoniae
E. Haemophilus influenzae type b

B. Neisseria meningitidis

Eculizumab is a recombinant humanised monoclonal antibody that specifically binds to terminal complement protein C5. Patients with C5 deficiency are at elevated risk of serious meningococcal infections and all patients being treated with eculizumab should receive a quadrivalent vaccine against the meningococcal strains A, C, W, and Y

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A 32-year-old male presents with a progressive worsening non-specific lethargy. 9 months ago, he had returned from an active holiday from New Zealand and now feels lethargic to the point that he can no longer work in his job as a computer programmer. In this period, he has been treated for two deep vein thromboses with low molecular heparin, the first initially attributed to his return flight from New Zealand. He reports three episodes of rose coloured urine over the past 4 months and intermittent episodes of abdominal cramps that his GP had diagnosed to be irritable bowel syndrome.

On examination, you note mild conjunctival pallor and jaundiced sclera. Respiratory, cardiovascular and abdominal examinations are unremarkable. His blood results are as follows:

Hb	76 g/l
MCV	92 fl
Platelets	276 * 10 /l9
WBC	4.1 * 10 /l9
Reticulocytes	18%
Haptoglobin	2 (normal range 41-165 mg/dL)
LDH	2128 (normal range 140-280 units/L)
Coombs' test	negative at 4 and 37 degrees

What is the definitive treatment for the underlying condition?

A. Packed red blood cell transfusion

B. Anti-retroviral treatment
C. Bone marrow transplant
D. R-CHOP chemotherapy
E. Intravenous iron replacement

C. Bone marrow transplant

This is a tricky clinical scenario with a number of red herrings: a young man in his 30s has presented with recurrent DVTs, episodes of haematuria, abdominal cramps and a blood picture suggestive of intravascular haemolysis (low haptoglobin, raised LDH) not secondary to an autoimmune cause (Coombs negative): there is thus an underlying red cell fragility predisposing to thrombosis, strongly suggestive of paroxysmal nocturnal haemoglobinuria (PNH). Note that haemoglobinuria is not restricted to night-time alone. The majority of patients present in their 30s with thromboses being the most common cause of death.

PNH is caused by an underlying reduced CD 59 on the red cell surface, leading to increased susceptibility to complement lysis. Complications can present following the release of haemoglobin, such as pulmonary hypertension, dystonia and renal impairment while PNH can overlap with aplastic anaemia and myelodysplasia. PNH patients are managed by blocking complement lysis with eculizumab and red cell transfusions but the only curative solution is allogenic bone marrow transplantation.

Question 39 of 191

A 24-year-old female presents with severe abdominal pain. This is her fourth presentation this year. She was previously told that the abdominal pain was medically unexplained. On examination you note peripheral neuropathy of her lower limbs. Her blood pressure is 160/110 mmHg and heart rate 125 beats per minute.

Blood results are as follows:

Hb	115 g/l	Na +	132 mmol/l
Platelets	468 * 10 /l 9	K +	3.8 mmol/l
WBC	14.2 * 10 /l 9	Urea	8.6 mmol/l
Neuts	10.8 * 10 /l 9	Creatinine	72 µmol/l
Lymphs	1.6 * 10 /l 9	CRP	28 mg/l
Eosin	0.2 * 10 /l9		
Urine	Increased levels of delta aminolevulinic acid and porphobilinogen		

What treatment is indicated?

A. Dimercaprol
B. Penicillamine
C. Dimercaptosuccinic acid (DMSA)
D. Haem arginate
E. Supportive management

D. Haem arginate

IV haem arginate can be used to treat flares of acute intermittent porphyria

The clinical features and laboratory data are suggestive of acute intermittent porphyria (AIP). This is one of the hereditary hepatic porphyrias. Its inheritance is autosomal dominant. The deficient enzyme is porphobilinogen deaminase (PBGD). A deficiency of PBGD is not sufficient by itself to produce AIP, and other activating factors must also be present. These include hormones, drugs and dietary changes.

Hematin and heme arginate is the treatment of choice during an acute attack of AIP. Heme is not a curative treatment, but can shorten attacks and reduce the intensity of an attack.

Dimercaprol, penicillamine and dimercaptosuccinic acid (DMSA) can be used to treat lead toxicity. Lead toxicity can present similarly to AIP (e.g. abdominal pain and peripheral neuropathy). In lead poisoning we would expect increased urinary coproporphyrin.

Question 40 of 191

A 30-year-old woman presents to the emergency department with severe, progressive abdominal pain over the past day. The pain is accompanied by nausea, vomiting and diarrhoea. The patient recalls similar episodes in the past that progressed over a few days and lasted for a week. Temperature is 37°C, blood pressure is 140/100 mmHg, pulse is 120/min and respirations are 16/min.

On examination: minimal abdominal tenderness and rebound tenderness. She has a history of abdominal surgery for suspected appendicitis and biliary disease, neither of which was confirmed once inside the abdomen.

Which of the following will help to confirm the diagnosis?

A. Erythrocyte porphyrins
B. Faecal porphyrins
C. Plasma porphyrins
D. Urine porphobilinogen
E. Urine porphyrins

D. Urine porphobilinogen

In acute intermittent porphyria, urinary porphobilinogen is typically raised

This patient has acute intermittent porphyria, which classically presents with neurovisceral symptoms which can mimic an acute abdomen. This mimicry occurs because the abdominal pain is produced by a nerve problem rather than inflammation, hence why exploratory surgery is uneventful. In long-standing cases, patients may have damage to their motor nerves resulting in upper limb weakness.

Question 41 of 191

A 40-year-old woman of Mediterranean descent was found to be anaemic during a workup for fatigue. Past medical history includes hypothyroidism, which is currently well controlled on 125mcg levothyroxine, and hypertension for which she takes amlodipine 5mg.

She denies any recent weight loss or change in bowel habits and her periods remain regular and are no heavier than normal. Blood tests results showed:

Hb	85g/l	115-165g/l
MCV	60fL	79-95fL
Iron	32nmol/L	13-32nmol/l
Ferritin	250µg/l	11-307µg/l

TIBC	50µmol/l	45-70µmol/l
Folate	2.5µg/l	3.1-19.9µg/l
B12	253ng/l	145-910ng/l

Which test is most likely to identify the underlying cause of her anaemia?

A. Anti-tissue transglutaminase (anti-tTG) antibodies
B. Colonoscopy
C. Prussian blue stain
D. Haemoglobin electrophoresis
E. Blood film

D. Haemoglobin electrophoresis

Disproportionately low MCV think thalassaemia

The differential diagnosis for microcytic anaemias includes iron deficiency anaemia (IDA), thalassaemia, and sideroblastic anaemia. Colonoscopy is used to investigated unexplained IDA but serum iron and ferritin levels were raised in this patient, thus excluding IDA.

The disproportionately low MCV compared with haemoglobin levels points towards thalassaemia where iron and ferritin levels can often be normal or high. Whilst a blood film would aid the diagnosis, HbA2 >3.5% on haemoglobin electrophoresis is diagnostic.

Prussian blue stains are used in the diagnosis of sideroblastic anaemia but one would expect significantly raised iron levels and reduced TIBC.

Anti-tTGs are used in the diagnosis of coeliac disease which often causes a mixed iron and folate deficiency. Whilst folate levels are low in this patient, this can also be explained by a chronic background level of haemolysis in thalassaemia and the other results are not in keeping with a coeliac picture.

Question 42 of 191

A 46-year-old man with a diagnosis of chronic hepatitis C is reviewed in hepatology clinic. He complains of 3 weeks of lethargy and generalised muscle pain.

On examination there are erythematous macules and purpuric papules on both lower limbs with some small areas of ulceration. Light touch and pain sensation is reduced in the toes bilaterally.

What is the most likely cause of these symptoms?

A. Eosinophilic granulomatosis with polyangiitis
B. Leukocytoclastic vasculitis
C. Granulomatosis with polyangiitis
D. Cryoglobulinaemia
E. Microscopic polyangiitis

D. Cryoglobulinaemia

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

A vasculitic rash and neuropathy in a patient with hepatitis C is suggestive of cryoglobulinaemia.

Small-vessel vasculitides can all cause neuropathy, however the association with hepatitis C makes cryoglobulinaemia most likely.

Patients with eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome) typically present with a history of allergic rhinitis and asthma. The disease progresses to eosinophilic infiltrative disease (eg, eosinophilic pneumonia or gastroenteritis) and systemic medium- and small-vessel vasculitis with granulomatous inflammation.

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis has a spectrum of presentations but often includes chronic sinusitis (failure to respond to conventional treatment is suggestive). Rhinitis and epistaxis occur in 22% and 11% of patients with GPA, respectively.

Question 43 of 191

A 65-year-old man attends the Emergency Department with a one-month history of persistent left-sided chest pain that is unresponsive to analgesia. He describes the pain as a constant ache, which does not worsen with exertion or radiate elsewhere. His medical background includes hypertension and diabetes, and he has a significant smoking history. His current medication regimen comprises enalapril, metformin, vildagliptin, and glimepiride.

Hb	110 g/L	Male: (135-180)
Platelets	210 * 10 /L 9	(150 - 400)
WBC	6.4 * 10 /L 9	(4.0 - 11.0)
Calcium	2.8 mmol/L	(2.1-2.6)
Na +	138 mmol/L	(135 - 145)
K +	4.4 mmol/L	(3.5 - 5.0)
Urea	7.2 mmol/L	(2.0 - 7.0)
Creatinine	235 µmol/L	(55 - 120)

No cardiac abnormalities were detected on ECG or echocardiography.

What is the most appropriate imaging modality for this patient?

A. Bone scan
B. Chest x-ray
C. PET-CT
D. Skeletal survey
E. Whole body MRI

A. Whole body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

Whole body MRI is the correct answer. The constellation of symptoms, including left-sided chest pain (bony aches), anaemia, hypercalcaemia, and renal impairment, should prompt consideration of multiple myeloma. Whole-body MRI is the recommended modality for diagnosis when multiple myeloma is suspected, as per NICE and BSH guidelines. Diagnostic features of myeloma on MRI include a diffuse pattern of bone marrow involvement and numerous focal lesions throughout the skeleton. These lesions typically present with a 'salt-and-pepper' appearance due to varying signal intensities caused by active myeloma cells and fatty marrow replacement.

Bone scan is not the appropriate choice. Although bone scans use a radioactive tracer to evaluate bone metabolism, they are limited in detecting small focal lesions and do not adequately assess bone marrow involvement in multiple myeloma. Furthermore, they may demonstrate nonspecific uptake in other conditions affecting bone remodelling and repair.

Chest x-ray, while capable of revealing osteolytic lesions, does not provide sufficient information to differentiate between multiple myeloma and metastatic disease; thus, it is not advocated for definitive diagnosis.

PET-CT, although an alternative diagnostic tool for patients with newly diagnosed nonsecretory or oligo secretory multiple myeloma or those presenting with the extramedullary disease, lacks sufficient evidence to support its routine use in all cases of newly diagnosed multiple myeloma. One limitation is the potential for high false positive and false negative findings rates.

Skeletal survey is less sensitive than CT, MRI, and PET/CT; therefore, it is considered suboptimal and is not advisable in this clinical scenario.

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An 18-year-old woman presents to the emergency department with dark urine. She had recently been diagnosed with 'mono' following a sore throat confirmed by swab testing, originally becoming unwell nine days ago. She had been recovering and was starting to feel well but then noticed passing dark urine after having a walk outside in the park but she started to return after it started to rain heavily and she became very cold. She also had abdominal cramping sensation. She has no other past medical history, takes no medication apart from the oral contraceptive pill, and has no allergies.

Blood tests:

Hb	101 g/l
Platelets	379 * 10 /l9
WBC	5.1 * 10 /l9
Bilirubin	43 µmol/l
ALP	161 u/l
ALT	15 u/l
Blood film	spherocytes

What is the most appropriate investigation to establish a diagnosis?

A. Hepatitis C serology
B. Syphilis serology
C. Anti-nuclear antibody
D. Direct Coombs test
E. ESO titre

D. Direct Coombs test

Paroxysmal cold haemoglobinuria should be confirmed with urinary heamosiderin

This is a young patient who has developed dark urine associated with exposure to going outside, implying exposure to cold. This has been associated with abdominal cramps and following a recent viral infection, most likely with Ebstein-Barr virus. In addition, blood tests show anaemia, elevated bilirubin and spherocytes. This implies haemolysis, and the history suggests that the haemolysis is associated after cold exposure. This history suggests is typical for paroxysmal cold haemoglobinuria. Paroxysmal cold haemoglobinuria is due to cold-reacting IgG causing complement fixation leading to haemolysis.

Diagnosis is best established with direct Coombs test to demonstrate the intravascular nature of haemolysis. Further testing can demonstrate the presence of temperature specific IgG antibodies which react to red blood cells below 37 degrees C and cause hemolysis on re-warming. Syphilis was historically associated with this condition, but only in tertiary syphilis which such a young patient is unlikely to have. Determining ESO titre to establish the viral infection is unlikely to be helpful in the current situation, and whilst hepatitis C is associated with cryoglobulinaemia it is not associated with paroxysmal cold haemoglobinuria. In older patients, paroxysmal cold haemoglobinuria can be associated with auto-immune conditions, making ANA a useful screening test, but there is no chronic history suggesting a prolonged autoimmune condition.

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A 74-year-old man attends with worsening fatigue and shortness of breath. A systematic enquiry was otherwise unremarkable. He was treated with radical chemo-radiotherapy for metastatic squamous cell carcinoma 5 years ago.

Blood results are as follows:

Hb	72 g/L	Male: (135-180)Female: (115 - 160)
Platelets	42 * 10 /L 9	(150 - 400)
WBC	2.1 * 10 /L 9	(4.0 - 11.0)
Neuts	0.4 * 10 /L 9	(2.0 - 7.0)
Lymphs	0.6 * 10 /L 9	(1.0 - 3.5)
Mono	1.0 * 10 /L 9	(0.2 - 0.8)
Eosin	0.1 * 10 /L 9	(0.0 - 0.4)
Blood film	Occasional hypogranular and hypolobulated neutrophil; Blasts 8% of all nucleated cells	

What is the most likely diagnosis?

A. Acute lymphoblastic leukaemia
B. Acute myeloid leukaemia
C. Metastatic infiltration
D. Myelodysplastic syndrome
E. Myelofibrosis

D. Myelodysplastic syndrome

Pancytopaenia 5 years post-chemotherapy/radiotherapy → ?myelodysplastic syndrome

Myelodysplastic syndrome is correct. The patient most likely has therapy-related myelodysplastic syndromes (t-MDS) which is defined as MDS occurring as a complication of cytotoxic chemotherapy and/or radiation. The median onset of occurrence is 5 years post-chemotherapy (however this can vary widely with the type of chemotherapy given). The blood film appearances of hypogranular and hypolobulated neutrophils are classic of MDS. The presence of myeloblasts is also in keeping with this condition, and since the blast count is < 20% on peripheral blood the diagnosis is MDS rather than acute myeloid leukaemia. The patient requires an urgent bone marrow aspirate and trephine for morphology, cell markers, and cytogenetics.

Acute lymphoblastic leukaemia is incorrect. Acute lymphoblastic leukaemia (ALL) is rare in adults. It is predominantly a disease of children. The blood film appearances

are not in keeping with ALL which would present with lymphoblasts and the absence of dysplasia in the myeloid lineage.

Acute myeloid leukaemia is incorrect. The peripheral blast count is < 20% confirming a diagnosis of MDS. Acute myeloid leukaemia (AML) is characterised by a peripheral blast count > 20%. It is important to note that the main risk of MDS is transformation to AML.

Metastatic infiltration is incorrect. Metastatic infiltration would be characterised by leukoerythoblastosis and teardrop poikilocytes on the blood film.

Myelofibrosis is incorrect. Myelofibrosis would also be characterised by leukoerythoblastosis and teardrop poikilocytes on the blood film.

Question 46 of 191

A 45-year-old gentleman has a diagnosis of renal cell carcinoma and is booked for a nephrectomy in four days time. He presents with an acutely swollen, tender left calf and a diagnosis of deep vein thrombosis is made, with the ultrasound report describing a clot extending to the femoral vein.

Which management is most appropriate?

A. Low molecular weight heparin and IVC filter insertion
B. Low molecular weight heparin
C. Warfarin
D. Apixiban
E. None

A. Low molecular weight heparin and IVC filter insertion

If a diagnosis of DVT is made less than 7 days before surgery, an IVC filter must be inserted pre-op

This gentleman has a malignancy that needs urgent operative management. An IVC filter should be inserted pre-operatively to bridge the operative period when low molecular weight heparin will be held.

The British Society of Haematology recommends that 'IVC filters should be considered in any preoperative patient with recent VTE (within 1 month) in whom anticoagulation must be interrupted'.

Whilst DOACs such as apixaban are now recommended first-line for venous thromboembolism they would be less suitable as surgery is planned in 4 days time.

Question 47 of 191

A 34-year-old woman presents to the emergency department with fever and bruising. She has no past medical history and does not take any regular medications. She does not smoke or drink alcohol and works as an accountant.

Observations:

- Heart rate 94 beats per minute
- Temperature 38.1ºC
- Blood pressure 170/101 mmHg
- Respiratory rate 18/minute
- Oxygen saturations 96% on room air

On examination, there is no meningism. You note that she is jaundiced but there are no signs of chronic liver disease. There are scattered petechiae on her arms, legs and abdomen.

Bloods tests:

Hb	72 g/L	Male: (135-180)Female: (115 - 160)
MCV	104fL	(80-96)
Platelets	33 * 10 /L	(150 - 400)
WBC	4.6 * 10 /L	(4.0 - 11.0)
Na	136 mmol/L	(135 - 145)
K	4.2 mmol/L	(3.5 - 5.0)
Urea	9.2 mmol/L	(2.0 - 7.0)
Creatinine	155 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	53 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	24 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	36 g/L	(35 - 50)
Prothrombin time	11 seconds	(10-14)
Blood film		schistocytes
ADAMTS13 enzyme		absent

Urinalysis:

Protein	++
Blood	++
Leucocytes	+
Nitrites	-ve
Glucose	-ve

Based on the likely diagnosis, what treatment is most likely to be effective?

A. Antibiotics
B. Antiplatelet therapy
C. High dose intravenous steroids
D. Intravenous labetalol
E. Plasma exchange

E. Plasma exchange

TTP - plasma exchange is first-line

Plasma exchange is correct. The patient has thrombotic thrombocytopenic purpura as evidenced by fever, thrombocytopenia, renal failure, microangiopathic haemolytic anaemia (jaundice, schistocytes) and absent ADAMTS13 enzyme activity. Haematoproteinuria is also common in this condition. The first-line treatment for this condition is plasma exchange (PEX), which removes inhibitory antibodies and replenishes the deficient protease.

Antiplatelet therapy is incorrect. While this is a thrombotic condition, there is a risk of haemorrhage with antiplatelet treatment.

High dose intravenous steroids is incorrect. Steroids are sometimes administered in this condition but have no proven benefit over PEX alone.

Intravenous labetalol is incorrect. While the patient is hypertensive, the blood pressure is not so high that we would label this as

malignant hypertension, which is a differential for a cause of microangiopathic haemolytic anaemia.

Antibiotics are not the right answer. While no one would criticise someone for administering antibiotics to someone with a petechial rash and fever, on the basis that it could be meningococcal septicaemia, antibiotics have no role in the management of TTP and may even worsen the condition.

Question 48 of 191

A 24-year-old female presents to the emergency department with severe abdominal pain which had developed over for the last few hours. The pain was central, severe and stabbing in nature associated with vomiting. She was in hysterics and was extremely agitated and confused. Past medical history included asthma and depression. Two days earlier she had seen her GP for dysuria and been prescribed trimethoprim.

She was a student studying chemistry at university and had recently been out late several nights drinking excess alcohol to celebrate passing her exams. On examination, she was unwell, extremely clammy, distressed with generalised abdominal tenderness and weakness in both legs with areflexia. Heart sounds and chest were clear. Observations showed a blood pressure 190/100 mmHg, heart rate 126/min, regular and temperature 37.9ºC.

Which investigation is most likely to be diagnostic?

A. Urinary catecholamines
B. Abdominal ultrasound
C. Urinary porphobilinogen
D. Lumbar puncture
E. Blood cultures

C. Urinary porphobilinogen

In acute intermittent porphyria, urinary porphobilinogen is typically raised

This patient has acute intermittent porphyria (AIP). AIP is the most common type of porphyria. AIP is an autosomal dominant condition caused by a genetic mutation in the gene encoding the enzyme porphobilinogen (PBG) deaminase on chromosome 11. The condition is more common in females than males and usually occurs between the ages 14-30 years. Porphyrias occur due to a problem within the haem biosynthesis. Defective PBG deaminase causes PBG to accumulate and this can be found in the urine. Attacks are usually precipitated by drugs, alcohol, fasting and sepsis. This patients attack has been caused by a combination of antibiotic use and alcohol intake.

Patients most commonly present with gastrointestinal symptoms (most commonly severe abdominal pain) neurological symptoms (autonomic dysfunction, peripheral motor neuropathies, areflexia, delirium, seizures, coma) and psychiatric symptoms such as common. Observations commonly show tachycardia and hypertension. Fever can be present. Most patients are completely free of symptoms between attacks.

The treatment for acute attacks of porphyria is to decrease haem synthesis and reduce the production of porphyrin precursors. Withdrawal of culprit medication is essential. A high-calorie intake and high doses of glucose can help inhibit haem synthesis and are useful for the treatment of mild attacks. In severe attacks, intravenous haematin is used. Pain is treated with narcotics. Beta blockers can be used to treat tachycardia and hypertension.

Advice can be obtained from National Acute Porphyria Centres: Cardiff, Kings College Hospital, London and Cambridge.

Question 49 of 191

A 22-year-old man attends with progressive tiredness over the past week. A systematic enquiry was otherwise unremarkable. He has a past medical history of hereditary spherocytosis. His regular medications include folic acid however he states that he often forgets to take this. On examination, you note 5cm splenomegaly.

Blood results are as follows:

Hb	55 g/L	Male: (135-180)Female: (115 - 160)
Platelets	142 * 10 /L 9	(150 - 400)
WBC	14.2 * 10 /L 9	(4.0 - 11.0)
Reticulocytes	0.2 %	(0.5 - 1.5)
Direct antiglobulin test (DAT)	Negative	
Bone marrow examination	Marked erythroid hypoplasia and occasional giant erythroblasts	

Blood results from the clinic 3 months ago are as follows:

Hb	105 g/L	Male: (135-180)Female: (115 - 160)
Reticulocytes	5.8 %	(0.5 - 1.5)

What is the most likely explanation?

A. Acute erythroblastic leukaemia
B. Folic acid deficiency
C. Haemolytic crisis
D. Parvovirus infection
E. Splenic sequestration crisis

D. Parvovirus infection

Parvovirus infection may trigger an aplastic crisis in patients with hereditary spherocytosis

Parvovirus infection is correct. Of note, the patient has significant reticulocytopaenia suggestive of bone marrow failure. Two of the commonest causes of this would include infection (e.g. Parvovirus) and megaloblastic anaemia (e.g. B12 and folate deficiency). In health, the usual life span of a red cell is approximately 120 days. However in conditions such as hereditary spherocytosis (HS), due to premature destruction by the spleen, the lifespan could be as low as 10- 30 days. Thus acute insults to the bone marrow can manifest much more rapidly in the peripheral blood. Acute parvovirus B19 infection can cause a transient erythroid hypoplasia as demonstrated on the bone marrow results in this case. In healthy populations this would unlikely cause more than mild anaemia, however, in patients with chronic haemolytic states (e.g. red cell membrane disorders and haemoglobinopathies), the effects can be much more rapid and profound as demonstrated in this case.

Acute erythroblastic leukaemia is incorrect. The giant erythroblasts within the bone marrow are indicative of acute parvovirus infection, not leukaemia.

Folic acid deficiency is incorrect. Patients with HS have chronic low-grade haemolysis and therefore an increased red cell turnover. Since folic acid is essential for haematopoiesis, all patients with HS should continue on lifelong folic acid replacement. This is even more essential in a haemolytic crisis. Importantly this remains the case even when folic acid levels are normal. Although the patient, in this case, has poor compliance with folic acid, the bone marrow examination is more suggestive of acute parvovirus infection rather than megaloblastic anaemia.

Haemolytic crisis is incorrect. The presence of a marked reticulocytosis would be suggestive of a haemolytic crisis. However, it would be important to compare this to the patient's baseline reticulocyte count since patients with hereditary spherocytosis will often have chronic reticulocytosis due to low-grade haemolysis of spherocytes. In this case, the patient's reticulocyte count is low, making a haemolytic crisis less likely.

Splenic sequestration crisis is incorrect. Although the patient has mild splenomegaly, this would be expected due to the chronic haemolytic state associated with hereditary spherocytosis. A splenic sequestration crisis would present with a marked and painful enlargement of the spleen.

Question 50 of 191

A 35-year-old male Caucasian presents to the emergency department. He was asked to come to hospital after his GP noticed that his recent community blood tests showed severe anaemia. He attended his GP two days ago due to feeling increasingly tired and therefore the GP did routine blood tests for him. Apart from increasing fatigue and shortness of breath on exertion he had noticed nothing wrong. He had no past medical history apart from appendectomy when he was 20 years old and has recently significantly increased his exercise in an attempt to loose weight, and developed severe muscle aches, for which he has started to take diclofenac regularly. He denies any pain currently. On examination he is mildly jaundiced, has no stigmata of liver disease and his abdomen is soft without tenderness.

Blood tests:

Hb	96 g/l
Platelets	357 * 10 /l9
WBC	4.8 * 10 /l9
Blood film	spherocytosis
Na +	138 mmol/l
K +	4.9 mmol/l
Urea	4.7 mmol/l
Creatinine	79 µmol/l
Bilirubin	58 µmol/l
ALP	188 u/l
ALT	26 u/l

Further investigations are pending.

What is the most likely diagnosis?

A. G6PD deficiency
B. Warm autoimmune haemolytic anaemia
C. Peptic ulcer disease
D. Sickle-cell anaemia
E. Thalassaemia

B. Warm autoimmune haemolytic anaemia

Warm autoimmune haemolytic anaemia can be confirmed with the presence of anaemia, spherocytes on blood film and positive direct Coombs test for IgG or C3d

This is a patient who has developed symptomatic anaemia and jaundice following taking diclofenac, and has no symptoms of gastric irritation or signs of epigastric tenderness. Furthermore, the presence of elevated bilirubin suggests a haemolytic cause for the anaemia. These factors make peptic ulcer disease less likely.

Warm autoimmune haemolytic anaemia is the most likely explanation due to the evidence of haemolysis occurring following the administration of a drug known to cause this problem, and the presence of spherocytes supports this as well, but confirmation would be with a positive direct Coombs test.

G6PD deficiency is a cause for acute haemolytic anaemia but is more common in those of African ancestry and occurs typically after oxidating drugs such as primaquine.

Sickle-cell anaemia is very unlikely in a Caucasian patient and is also unlikely to be diagnosed at this age, and also would likely have a history of sickle-cell crisis.

Thalassemia is a disorder of globin genes causing ineffective erythropoiesis and haemolysis, endemic in the Mediterranean region and Africa. The blood film would be expected to show microcytosis and target cells rather than spherocytosis, and there is no evidence of extramedullary haematopoiesis.

Question 51 of 191

A 65-year-old man attends the clinic with a three-month history of generalised, dull-aching bone pain and increased fatiguability. He has a history of hypertension, which is well-controlled with amlodipine 10 mg daily. On examination, he exhibits pallor and has bruises and petechiae on his shins and forearms. Laboratory results are attached.

Hb	7.6 g/L	Male: (135-180)
Platelets	39 * 10 /L 9	(150 - 400)
WBC	3.1 * 10 /L 9	(4.0 - 11.0)
Calcium	3.1 mmol/L	(2.1-2.6)
Creatinine	140 µmol/L	(55 - 120)

What is the most appropriate next investigation to determine the cause of this patient's bone pain?

A. MRI spine
B. Whole body MRI
C. Whole body isotope bone scan
D. Whole body low dose CT scan
E. X-ray skull and spine

B. Whole body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

Whole body MRI is the preferred initial imaging modality for detecting myeloma-related bone disease and extra-medullary plasmacytomas. The clinical features of bone pain, fatigue,

anaemia, thrombocytopenia, deranged creatinine, and hypercalcaemia in an older man are suggestive of multiple myeloma. It is standard practice to offer imaging to all patients with a suspected diagnosis of myeloma to investigate potential bone involvement, and a whole-body MRI is the most suitable investigation. This imaging modality can detect both lytic lesions and bone marrow infiltration, which are characteristic of multiple myeloma.

Whole body low dose CT scan is recommended as the first-line alternative for imaging in patients with myeloma in instances where an MRI is contraindicated due to the presence of a pacemaker, metallic heart valves, or aneurysm clips. For comprehensive assessment in this context, a whole-body MRI would be necessary rather than just an **MRI spine**.

A **whole body isotope bone scan** is not indicated for initial screening of myeloma-related bone disease. An isotope bone scan relies on osteoblastic activity and may yield a false negative result, particularly in cases where bone turnover is not high.

An **x-ray skull** is not a primary imaging choice for evaluating myeloma-associated bone pathology. While a raindrop skull on an x-ray can support the diagnosis of multiple myeloma, it is not sensitive or specific enough to be used as a primary diagnostic tool.

Question 52 of 191

A 20-year-old female complains of feeling tired. She has no past medical history and takes no regular medications.

The following blood tests were obtained:

Hb	84g/L
MCV	70fL
WBC	8x10^9/L
Platelets	460x10^9/L

Blood film analysis comments on hypochromic anaemia with pencil cells, target cells, acanthocytes and Howell Jolly bodies.

What is the most likely diagnosis?

A. Sickle cell anaemia
B. Hereditary spherocytosis
C. Thalassaemia trait
D. Iron deficiency anaemia
E. Coeliac disease

E. Coeliac disease

The blood film shows hypochromic anaemia with the presence of pencil cells that indicates the patient has iron deficiency anaemia. Target cells, acanthocytes and Howell Jolly bodies are features of hyposplenism. Iron deficiency and functional hyposplenism are both seen in coeliac disease, which is therefore the most likely unifying diagnosis. Thalassaemia trait is associated with mild reduction in haemoglobin, low MCV and low MCH; there would not be evidence of hyposplenism on the film in thalassaemia trait. Hereditary spherocytosis is due to a deficiency in spectrin, which leads to an abnormal red blood cell cytoskeleton. The film would show spherocytic red blood cells and reticulocytes. In sickle cell anaemia MCV is usually normal and sickle cells would be seen on the blood film.

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A 34-year-old man presents to the emergency department with abdominal pain. He has a background of multiple previous attendances with similar symptoms, which typically last for 3-7 days and then resolve. On a previous occasion, he underwent an exploratory laparoscopy, which did not identify a cause. He has a past medical history of depression. He takes citalopram. He does not smoke cigarettes or drink alcohol. He is a ceramicist. He has been under a lot of stress at work recently.

His observations are heart rate 111 beats per minute, blood pressure 153/74 mmHg, respiratory rate 18/minute, oxygen saturation 96% on room air and temperature 37ºC.

Examination reveals a soft and non-tender abdomen with normal bowel sounds. There are no abnormalities of the external genitalia. A bilateral foot drop is noted on neurological examination.

Blood tests:

Hb	136 g/L	Male: (135-180)Female: (115 - 160)
Platelets	189 * 10 /L 9	(150 - 400)
WBC	5.6 * 10 /L 9	(4.0 - 11.0)
Na +	129 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	8.2 mmol/L	(2.0 - 7.0)
Creatinine	89 µmol/L	(55 - 120)
CRP	23 mg/L	(< 5)
Lactate	1.2 mmol/L	(0-2)

A urine sample is requested and it is noted to turn dark red when left standing. Porphobilinogen is increased in the urine.

Plain radiography of the abdomen and chest are normal.

Based on the likely diagnosis, what is the most appropriate treatment?

A. Chelation therapy
B. IV hydrocortisone
C. Supportive treatment only
D. 5% dextrose
E. Haem arginate and 10% dextrose

E. Haem arginate and 10% dextrose

IV haem arginate can be used to treat flares of acute intermittent porphyria

Haem arginate and 10% dextrose is the correct answer. This presents with features suggestive of acute intermittent porphyria (unexplained abdominal pain, depression, neuropathy, hyponatraemia, hypertension, tachycardia, red urine) and increased levels of urine porphobilinogen. Intravenous glucose inhibits the activity of aminolaevulinic acid synthase (an enzyme in the haem pathway). This reduces the overproduction of porphyrins. More hypotonic dextrose infusions should be avoided as they may worsen hyponatraemia. Haem arginate itself inhibits 5-aminolevulinic acid, which is another component in the porphyrin synthesis pathway. While the randomized control evidence of is lacking for this treatment, it is felt that patients typically respond well to this treatment and it should be given early in a severe attack.

5% dextrose is incorrect. Hypotonic dextrose solutions should be avoided as they may worsen hyponatraemia.

Chelation therapy is incorrect. Lead poisoning is a mimic of acute intermittent porphyria and can cause unexplained abdominal pain and neuropathy. However, the key distinction is that urine levels of porphobilinogen will not be increased in this condition. The diagnosis is typically confirmed by measuring levels of lead in the blood.

IV hydrocortisone is incorrect. Addison's disease can cause abdominal pain and hyponatraemia but you would expect hypotension rather than hypertension and the urinary findings are not typical of this condition.

Supportive treatment only is incorrect. This patient has a significant attack of acute intermittent porphyria with evidence of raised urinary porphobilinogen and motor neuropathy. This indicates a need for treatment with the above regimen.

Question 54 of 191

A 70-year-old man is referred to the haematology clinic by his general practitioner with anaemia. He has experienced progressive fatigue and shortness of breath for four months. On further questioning he also describes waking up at night soaked in sweat on one or two nights per week for the last month. His weight is stable. He has a past medical history of hypertension and COPD.

On examination he is pale. His heart sounds are normal and his chest is clear.. He has no ankle oedema and JVP is not raised. His abdomen is soft and he has splenomegaly 3cm below the costal margin with no hepatomegaly.

Test results sent with him by his GP are a follows:

Hb	92 g/l	Na +	143 mmol/l
Platelets	143 * 10 /l 9	K +	3.7 mmol/l
WBC	4 * 10 /l 9	Urea	7 mmol/l
Neuts	2 * 10 /l 9	Creatinine	86 µmol/l
Lymphs	1 * 10 /l 9	CRP	5 mg/l

Blood film: Anisocytosis with mild hypochromia. Tear drop cells. Mild thrombocytopenia with no platelet clumping.

Chest x-ray: Mildly hyperexpanded lung fields. No focal consolidation. No masses or lymphadenopathy.

Upper GI endoscopy & colonoscopy: Normal

Presence of which mutation is required to confirm the likely diagnosis?

A. BCR-ABL
B. BCL2
C. C-MYC
D. JAK2
E. TP53

D. JAK2

This gentleman has B symptoms, anaemia and splenomegaly in the presence of characteristic tear drops cells on the blood film, making myelofibrosis the most likely diagnosis. The British

Committee for Standards in Haematology list several mutations which together with these

symptoms and fibrosis on bone marrow form the diagnostic criteria. The most common of these is

JAK2.

Presence of BCR-ABL is diagnostic for CML. BCL2 and TP53 mutations are seen in diffuse large B

cell lymphoma.

C-MYC mutations are seen in Burkitt's lymphoma.

Use of JAK inhibitors in the management of myelofibrosis: a revision of the British Committee for

Standards in Haematology Guidelines for Investigation and Management of Myelofibrosis 2012.

British Journal of Haematology, 2014;:167;418438.

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A 48-year-old male with hepatitis C is admitted to the acute medical assessment unit having noticed a significant reduction in his urine output over the last few days. Urinalysis revealed haematoproteinuria, and his blood results are as follows:

Hb	9.8 g/dl
Platelets	75 * 10 /l9
WBC	12.1 * 10 /l9
Na +	143 mmol/l
K +	5.4 mmol/l
Urea	18.9 mmol/l
Creatinine	205 µmol/l

A renal biopsy was subsequently performed and microscopy of the sample showed generally enlarged and hypercellular glomeruli with an increase in mesangial cellularity and matrix. A histological diagnosis of membranoproliferative glomerulonephritis is made.

What is the most likely underlying pathology for this finding?

A. Cryoglobulinaemia
B. Haemolytic uraemic syndrome
C. Hepato-renal syndrome
D. Systemic lupus erythematosus
E. Thrombotic thrombocytopaenic purpura

A. Cryoglobulinaemia

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

This gentleman presents with acute kidney injury secondary to membranoproliferative glomerulonephritis. All of the listed options are recognised causes of membranoproliferative glomerulonephritis, but the key to this question is the patient's history of hepatitis C which is known to be closely associated with cryoglobulinaemia.

Question 56 of 191

A 77-year-old man presents with a general decline in mobility, extreme lethargy, and weight loss. His admission blood tests show:

Hb	98 g/L	Male: (135-180)Female: (115 - 160)
Platelets	119 * 10 /L 9	(150 - 400)
WBC	3.8 * 10 /L 9	(4.0 - 11.0)

Na +	137 mmol/L	(135 - 145)
K +	4.4 mmol/L	(3.5 - 5.0)
Urea	6.1 mmol/L	(2.0 - 7.0)
Creatinine	73 µmol/L	(55 - 120)
Calcium	2.46 mmol/L	(2.1-2.6)

A CT TAP is performed:

No evidence of solid organ malignancy or bony lesions. Splenomegaly noted - clinical correlation advised.

Given the ongoing concern for malignancy, a myeloma screen is sent:

IgA	0.56 g/L	(0.64-2.97)
IgG	4.7 g/L	(5.8-15.4)
IgM	12.52 g/L	(0.71-2.3)
Serum electrophoresis	Shows a paraprotein band	
Paraprotein level	44g/L	
Serum immunofixation	IgM type kappa paraprotein	
Serum free kappa light chains	13.65mg/L	(3.30-19.40)
Serum free lambda light chains	18.09 mg/L	(5.71-26.30)
Serum kappa / lambda ratio	0.75	(0.26-1.65)

What is the most likely diagnosis?

A. Acute lymphoblastic leukaemia
B. Monoclonal gammopathy of uncertain significance
C. Multiple myeloma
D. Smouldering myeloma
E. Waldenstrom's macroglobulinaemia

A. Waldenstrom's macroglobulinaemia

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is the correct diagnosis. The patient presents with relatively non-specific symptoms; however, initial findings of pancytopenia and radiological evidence of splenomegaly are concerning for a haematological malignancy. Subsequent serological investigations revealing elevated serum free light chains and electrophoresis indicating a raised IgM level, alongside an IgM-type kappa paraprotein, strongly suggest Waldenstrom's macroglobulinaemia.

Acute lymphoblastic leukaemia (ALL) is not the appropriate diagnosis. ALL is characterised by the malignant proliferation of lymphoid progenitor cells and typically presents with lymphadenopathy and signs consistent with bone marrow infiltration by malignant clones, such as anaemia and thrombocytopenia. While initial blood tests may show leukocytosis, anaemia, and thrombocytopenia, elevated IgM levels (12.52 g/L) and an associated IgM-type kappa paraprotein indicate a monoclonal gammopathy rather than ALL. Lymphoid progenitor cells in ALL do not secrete immunoglobulins in large quantities; thus, the detection of a paraprotein band, specifically an IgM-type kappa paraprotein on serum electrophoresis, does not align with ALL but instead suggests plasma cell disorders such as Waldenstrom's macroglobulinaemia or multiple myeloma.

Monoclonal gammopathy of uncertain significance (MGUS) is also incorrect. Although MGUS with an IgM paraprotein could yield similar serum electrophoresis and immunofixation results to those observed in this case, MGUS is asymptomatic by definition—contrary to our patient who exhibits symptomatic anaemia. Furthermore, diagnostic criteria for MGUS stipulate that the paraprotein concentration must be below 30g/L; this patient's level exceeds this threshold at 44g/L. The combination of symptomatic presentation and a higher paraprotein level excludes MGUS as a diagnosis.

Multiple myeloma does not fit this clinical picture either. Defined by CRAB features (hypercalcaemia, renal failure, anaemia, bony lesions), multiple myeloma involves monoclonal plasma cell proliferation detectable via serum electrophoresis showing a paraprotein presence. However, an IgM-type kappa paraprotein is more indicative of Waldenstrom's macroglobulinaemia than multiple myeloma; the latter more commonly involves IgG or IgA production. Additionally, splenomegaly is less common in multiple myeloma cases. The absence of skeletal lesions further argues against multiple myeloma as a diagnosis here. While multiple myeloma can present with variable levels of serum free light chains depending on disease burden and subtype—a finding not prominent in this patient—the normal range kappa/lambda ratio observed supports Waldenstrom's macroglobulinaemia over multiple myeloma.

Smouldering myeloma, like smouldering forms of other malignancies, presents without symptoms or end-organ damage—which includes CRAB features or any indication of organ impairment—and typically involves either IgG or IgA rather than IgM paraproteins. Given that our patient has symptomatic anaemia, smouldering myeloma is ruled out as a diagnosis in favour of Waldenstrom's macroglobulinaemia which accounts for both the symptomatology and laboratory findings observed.

Question 57 of 191

A 35-year-old patient with known sickle cell disease presents to the emergency department with new onset of left arm and facial weakness. The symptoms began earlier in the day. He is normally very careful with his sickle disease and ensures he is well hydrated and avoids the cold. His wife admits that over the last few days he has been suffering from nausea and vomiting and diarrhoea after he had a takeaway meal 3 days ago, On examination he his observations are within normal parameters. He has slurred speech and an obvious left facial droop with forehead sparing. He has power of 0/5 in his left arm but is otherwise neurologically intact.

His blood test show:

Hb	100 g/l
Platelets	330 * 10 /l9
WBC	8.9 * 10 /l9
INR	1.0
Na +	138 mmol/l
K +	3.5 mmol/l
Urea	9.9 mmol/l
Creatinine	135 µmol/l
CRP	19 mg/L(<10)
Bilirubin	12 µmol/l
ALP	89 u/l
ALT	39 u/l
Albumin	39 g/l

He is seen by the stroke team who arrange an urgent CT head which is reported as normal.

What is the appropriate treatment for this gentleman?

A. Thrombolysis
B. Aspirin
C. Plasmapheresis
D. Methylprednisolone
E. Exchange transfusion

A. Exchange transfusion

Exchange transfusions are a way of reducing the number of sickle red cells and increasing the number of normal red cells, in order to improve oxygenation

This gentleman has a cerebral vaso-occlusive episode as a result of his sickle cell disease. The treatment of choice in these situations is urgent and aggressive exchange transfusion followed by transfusions to maintain HbS <30%. Thrombolysis and aspirin are not in the management guidelines for acute stroke in this situation.

Question 58 of 191

A 29-year-old man who is known to be HIV positive is reviewed. He has been taking anti-retroviral therapy for the past 2 years and has remained relatively well. Over the past few weeks however he has developed abdominal distension with some discomfort in the right iliac fossa. On examination a mass can be felt in the right lower quadrant. A biopsy shows a B cell lymphoma. Sheets of a medium sized lymphoid cells with high proliferative activity, forming a 'starry sky' appearance, are noted.

What cytogenic abnormality is most likely to be found?

A. t(11;14)
B. t(14;18)
C. t(8;14)
D. t(9;22)
E. t(11;18)

C. t(8;14)

Burkitt's lymphoma - t(8:14)

This patient has an immunodeficiency-associated Burkitt lymphoma

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A 27-year-old woman is admitted after developing dyspnoea associated with pleuritic chest pain. A D-dimer taken on admission is elevated and subsequent CTPA shows a pulmonary embolism. Her past medical history includes a giving birth to her son 12 months ago (full term, vaginal delivery) and anxiety. She reports that her 47-year-old mother has had two deep vein thromboses in the past 10 years.

Which one of the following is the most likely underlying cause?

A. Factor V Leiden
B. Antithrombin III deficiency
C. Antiphospholipid syndrome
D. Protein C deficiency
E. Prothrombin gene mutation

A. Factor V Leiden

Activated protein C resistance (Factor V Leiden) is the most common inherited thrombophilia

NICE would recommend testing for thrombophilia given the unprovoked venous thromboembolism and family history

Question 60 of 191

A 19-year-old man with hereditary spherocytosis is reviewed in the clinic. He was last admitted to the hospital some 6 months earlier for an acute haemolytic crisis related to parvovirus infection. He complains that he feels chronically tired and has persistent left upper quadrant pain and discomfort. Abdominal examination confirms splenomegaly.

Investigations:

Abdominal ultrasound scan reveals splenomegaly and a solitary gallstone visualised within the gallbladder.

Hb	90 g/l
MCV	101 fL
Platelets	301 * 10 /l9
WBC	7.1 * 10 /l9

Which of the following is the most appropriate intervention for him?

A. Prednisolone
B. Splenectomy
C. Cholecystectomy
D. Oral iron supplementation
E. IV iron supplementation

B. Splenectomy

Elective splenectomy is appropriate in a patient with hereditary spherocytosis who has recurrent anaemia

This patient has hereditary spherocytosis with evidence of chronic haemolysis. Although this patient doesn't yet have symptoms of cholecystitis they have evidence of possible pigment gallstone formation on the ultrasound scan and symptomatic splenomegaly. Coupled with the anaemia and raised MCV (suggestive of increased reticulocytes), this clinical picture points to elective splenomegaly as the most appropriate option, with vaccination at least against pneumococcus before the procedure is carried out.

Cholecystectomy is carried out where patients present with cholecystitis related to hereditary spherocytosis. Prednisolone may help stimulate red cell production in situations where there is an acute haemolytic crisis. There is no role for iron supplementation here. IV iron supplementation is usually considered for patients with chronic renal impairment.

Question 61 of 191

A 60-year-old woman presents to the clinic with a one-year history of generalised body pain and fatigue. She intermittently experiences epistaxis and bleeding gums. She underwent a fundoscopy for blurred vision, which showed retinal haemorrhages and dilated retinal veins. Examination reveals pallor and hepatosplenomegaly. Serum protein electrophoresis demonstrates a

sharp, narrow spike of monoclonal IgM. A skeletal survey is normal. A bone marrow biopsy is scheduled.

What are the expected findings of the bone marrow biopsy for this patient?

A. <10% infiltration of bone marrow with lymphoplasmacytic cells
B. <10% monoclonal plasma cells
C. >10% infiltration of bone marrow with lymphoplasmacytic cells
D. >10% monoclonal plasma cells with clock-face chromatin
E. Abnormal B cells

C. >10% infiltration of bone marrow with lymphoplasmacytic cells

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

> 10% infiltration of the bone marrow with lymphoplasmacytic cells is the typical bone marrow finding observed in patients with Waldenstrom's macroglobulinemia, which is the case here. The patient's presentation and investigations are consistent with Waldenstrom's macroglobulinaemia, a lymphoplasmacytic malignancy characterised by the secretion of a monoclonal IgM paraprotein. The disease typically presents with systemic symptoms such as fatigue and weight loss, hyperviscosity syndrome (e.g., blurred vision due to retinal haemorrhages), and hepatosplenomegaly.

< 10% infiltration of bone marrow with lymphoplasmacytic cells is typically observed in monoclonal gammopathy of undetermined significance (MGUS). The features such as anaemia, hepatosplenomegaly and hyperviscosity symptoms outlined in this scenario are rarely associated with MGUS; hence, this option is not applicable.

< 10% monoclonal plasma cells is incorrect because it is < 10% monoclonal plasma cells can be seen in MGUS. It is important to distinguish this condition from multiple myeloma. The lack of bony lesions and normal skeletal survey findings exclude multiple myeloma in this case. Additionally, IgM myeloma is exceedingly uncommon. **> 10% monoclonal plasma cells with clock-face chromatin** typify multiple myeloma; therefore this choice is incorrect.

Chronic lymphocytic leukaemia (CLL) represents another differential diagnosis characterised by **abnormal B cells** within the bone marrow. Monoclonal gammopathy is uncommon in CLL. Serum protein electrophoresis typically appears normal in CLL cases and only demonstrates abnormal protein spikes in approximately 15% of instances.

Question 62 of 191

A 28-year-old Afro-Caribbean male presents with a two-hour history of sudden onset left sided weakness. He denies any sensory involvement, dysarthria or dysphasia. He has a known history of sickle cell disease, with two previous episodes of transient ischaemic attacks and an episode of acute chest syndrome attack 10 days ago. On examination, he displays power of 1/5 in his left arm, 2/5 in his left leg, 5/5 in his right side. He reports no sensory disturbances, plantar responses are downgoing bilaterally, he is unable to perform finger-nose testing. He denies any illicit drug use, is a non-smoker and does not drink alcohol. He has no other past medical history. A hyperacute CT head demonstrates an area of acute ischaemia in the right internal capsule region.

What is the most appropriate immediate treatment?

A. Intravenous thrombolysis
B. Aspirin 300mg
C. Intravenous thrombolysis and mechanical thrombectomy
D. Exchange transfusion
E. Clopidogrel 300mg

D. Exchange transfusion

Exchange transfusions are a way of reducing the number of sickle red cells and increasing the number of normal red cells, in order to improve oxygenation

This patient has presented with an acute vaso-occlusive crisis on a background of known sickle cell disease. He is at high risk of an infarctive stroke given the background of previous TIAs (increased relative risk by 56 times) and a recent chest crisis within the past 2 weeks (increased relative risk by 7 times). The other risk factors include a high systolic pressure (RR 1.3 increase per 10mmHg) and

a low steady state haemoglobin (RR 1.9 per 1g/dL decrease)1. The management of an acute sickle infarct is different to that of thromboembolic stroke or atheromatous disease. The immediate aim is to reduce the proportion of HbS, either with immediate transfusion or optimally, with exchange transfusion. The latter reduces the concentration of HbS faster with a lower risk of transfusional volume overload, possibly resulting in increased blood viscosity and consequent pulmonary oedema.

Question 63 of 191

A 25 year old man presented to the Emergency Department with acute onset, rapidly progressive weakness in all the four limbs following a bout of severe colicky abdominal pain which lasted for 10 days but eventually subsided. The abdominal pain was located around the umbilicus, stabbing in nature, radiated towards the back, and was associated with nausea and intermittent constipation. Patient reports weakness originating in both arms then affecting both the lower limbs. He also complains of difficulty in closing his lips and eyes, and has uncontrolled salivation from the angles of the mouth. He denied any history of paraesthesia, sphincteric disturbances, epileptic fits or dark colored urine during any of the episodes. No definite history of any drug intake prior to both the episodes could be ascertained.

Physical examination revealed bilateral facial palsy of lower motor neuron (LMN) type together with flaccid quadriparesis which was more marked distally with bilateral wrist drop. Deep tendon reflexes were diminished in both upper and lower limbs. There was no sensory loss.

Initial lab values showed WBCs 8.9x10^9/L, Hemoglobin of 12g/L, Sodium of 132mmol/L, and ESR of 35mm/Hr. His temperature was 36.5 C and pulse 83/min. His blood pressure was 130/83 mm/Hg and oxygen saturations were 98% on air. A lumbar puncture was performed and CSF studies were normal.

Which of the following is most likely to be diagnostic?

A. CT scan with contrast of abdomen
B. MRI brain with contrast
C. Urine screen for Vanillylmandelic acid (VMA)
D. Urine screen for Aminolevulinic Acid (ALA) and Porphobilinogen (PBG)
E. Measurement of urinary and stool porphyrins

D. Urine screen for Aminolevulinic Acid (ALA) and Porphobilinogen (PBG)

n acute intermittent porphyria, urinary porphobilinogen is typically raised

Acute attacks of Acute Intermittent Porphyria (AIP) are often precipitated by drugs like barbiturates, sulfonamides, chloroquin, griseofulvin, diphenyl hydantoin and many other drugs, acute infections and over-indulgence in alcohol. Acute attacks are due to greatly increased activity of delta-aminolaevulinic acid synthetase. During acute attacks, the urine contains large amounts of porphobilinogen (PBG) and delta-aminolaevulinic acid (ALA) which, on standing, gives dark 'portwine' colour to the urine. Mental disturbances during acute episodes are of metabolic origin whilie neurological weakness of the extremities is due to focal demyelination and/or axonal degeneration of peripheral and autonomic nerves.

Onset of symptoms usually occurs in adolescence. Females are more commonly affected than males. The clinical picture is dominated by gastrointestinal and neurological manifestations. Symptoms during acute episodes usually comprise of severe colicky pain in the abdomen which may be diffuse or localized-usually to the umbilical or epigastric region and is often associated with nausea and vomiting and occasionally diarrhea. Diagnosis in such patients may be missed, unduly delayed or confused with acute surgical abdomen especially if neurological manifestations are lacking. Gastrointestinal manifestations are related to severe intestinal spasm due to autonomic dysfunction. Neurological manifestations comprise of flaccid paralysis, neuropsychiatric disturbances and rarely generalized epileptic fits. Paralysis may be confined to lower or upper extremities or may affect all the four limbs. It may be more marked proximally or distally or may be generalized and is due to predominant motor neuropathy. Sensory symptoms may also occur but objective sensory loss is unusual. Epileptic fits in AIP have been reported in about 15 to 20% cases. Bulbar paralysis and respiratory involvement can also occur and may threaten the life of the patient. Sphincteric disturbances are uncommon. Skin lesions are seldom seen.

Diagnosis of AIP should be suspected in any patient presenting with rapidly progressive flaccid paralysis with severe abdominal pain and history of passing dark reddish urine. Examination of the urine during acute attacks for PBG and ALA will help in establishing the diagnosis. In the patient in the above case, the diagnosis of AIP was based on clinical and urinary findings.

There is no specific treatment for porphyria and it is therefore very important to prevent the onset of acute attack. Treatment during acute episodes usually comprises symptomatic and general supportive measures for bulbar and respiratory paralysis, if it occurs. Chlorpromazine has been reported to be beneficial in relieving pain and other symptoms. Approximately 25% siblings of patients of AIP may be expected to have PBG in urine and therefore screening of siblings and other family members should be done. Prophylaxis in such cases as well as those known to clinically manifest AIP includes the avoidance of drugs known to precipitate the acute attacks as enlisted above.

Question 64 of 191

A 55-year-old man is referred by her GP to the haematology clinic. He reports a four-week history of night sweats and early satiety. On questioning, he elaborates and says that he has been feeling unwell for some time, but that he had just started work as a managing director and had attributed this to the added stress of his promotion.

On examination, he is pale with an unremarkable cardiovascular and respiratory exam. There is a fullness in the left upper quadrant which moves with inspiration and widespread small volume lymphadenopathy.

His blood tests are shown below:

Hb	100 g/L	Male: (135-180)Female: (115 - 160)
Platelets	117 * 10 /L 9	(150 - 400)
WBC	30.1 * 10 /L 9	(4.0 - 11.0)
Neuts	4.0 * 10 /L 9	(2.0 - 7.0)
Lymphs	25.0 * 10 /L 9	(1.0 - 3.5)
Mono	0.8 * 10 /L 9	(0.2 - 0.8)
Eosin	0.3 * 10 /L 9	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

A bone marrow biopsy shows lymphocytosis in a diffuse growth pattern.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis,

which of the following findings would suggest a poor prognosis?

A. Wild-type TP53
B. >2% mutated immunoglobulin heavy chain variable region
C. Deletion of 13q
D. Mutated TP53
E. < 20% expression of CD38 lymphocytes

D. Mutated TP53

TP53 mutation is associated with a poor prognosis in CLL

This patient has aggressive chronic lymphocytic leukaemia (CLL) with both constitutional symptoms and bone marrow failure, indicating the need for treatment. The chromosomal analysis may be used to guide treatment offers significant insights into prognostication.

The presence of a mutated TP53 is a poor prognostic marker, where a 'wild type' refers to an unmutated form and is a good prognostic marker. A >2% mutated immunoglobulin heavy chain variable region, deletion of 13q or < 20% expression of CD38 lymphocytes are good prognostic markers.

Question 65 of 191

A 26-year-old gentleman presents to haematology clinic one week prior to starting chemotherapy for acute myeloid leukaemia (AML). He is currently feeling fatigued, suffering from night sweats, and has chronic lower back pain. He is anxious to start treatment.His past medical history includes ankylosing spondylitis

and a clavicular fracture. His current medications include paracetamol and ibuprofen.

Blood tests:

Hb	113 g/l
Platelets	156 * 10 /l9
WBC	57 * 10 /l9
Na +	140 mmol/l
K +	3.6 mmol/l
Urea	4.2 mmol/l
Creatinine	63 µmol/l

What measure is the least useful to prevent tumour lysis syndrome?

A. IV fluids prior to chemotherapy
B. Urine alkalization
C. Prophylactic allopurinol
D. Prophylactic rasburicase
E. Stopping NSAID use

B. Urine alkalization

This patient has AML with a high white cell count and is about to start chemotherapy, and is therefore at high risk of tumour lysis syndrome (TLS).The key is to prevent TLS, which is done by ensuring good renal perfusion. Commonly this can be done by aggressive intravenous hydration prior to the start of treatment and stop NSAIDs, such as ibuprofen for this patient. Allopurinol and rasburicase both prevent uric acid accumulation and can, therefore, be used as well. Urine alkalization has not shown to be effective.

Question 66 of 191

A 50 year old woman was referred to haematology clinic for management of a persistent erythrocytosis that had been monitored by her General Practitioner over the previous 6 months. The patient was asymptomatic and in particular reported no headaches or visual changes. Past medical history was remarkable only for internal fixation of a tibial fracture sustained in a car accident 5 years previously. There is no strong family history of venous thrombosis or ischaemic heart disease. The patient took no regular medications and worked as an accountant. She is a lifelong non-smoker and drinks approximately 10 units of alcohol per week.

Following assessment at haematology, further investigations were requested as listed below.

Hb	# g/dl
Platelets	# * 10 /l
WBC	# * 10 /l
Haemoglobin	18.7 g / dL
White cell count	6.1* 10 /l
Neutrophils	3.5 * 10 /l
Lymphocytes	1.0 * 10 /l
Monocytes	0.7 * 10 /l
Eosinophils	0.4 * 10 /l
Basophils	0.5 * 10 /l
Platelets	276 * 10 /l
Packed cell volume	0.57
Urea	4.5 mmol / L
Creatinine	95 micromol / L
Sodium	142 mmol / L
Potassium	4.5 mmol / L
Ferritin	56 ng / mL
Albumin	35 g / L
Alkaline phosphatase	80 U / L
ALT	20 U / L
Bilirubin	18 micromol / L
JAK 2 V617F mutation	Postive
Serum erythropoietin	3 U / L (reference 0-19)

Blood film: no abnormality detected

Abdominal ultrasound: liver, hepatic duct system and gallbladder unremarkable; mild-moderate splenomegaly; kidneys and renal tract unremarkable

What is the appropriate management for the patient's erythrocytosis?

A. Aspirin and venesection with target PCV < 0.45
B. Aspirin and venesection with target PCV 0.45-0.50
C. Aspirin
D. Venesection with target PCV 0.45-0.50
E. Hydroxyurea

A. Aspirin and venesection with target PCV < 0.45

This patient has polycythemia vera as evidenced by the positive JAK 2 mutation, normal blood film, splenomegaly and low serum erythropoietin.

Management of polycythemia depends on the patient's risk of thrombosis. This patient has a low risk of thrombosis based on her age, absence of cardiac risk factors, normal white cell and platelet count and absence of hyperviscosity symptoms.

The mainstay of treatment of polycythaemia vera is aspirin and venesection. A target PCV < 0.45 has been shown to have a significantly lower rate of death from cardiovascular disease and major thrombosis than target PCV 0.45-0.50. Treatment with aspirin reduces the risk of non-fatal myocardial infarction, non-fatal stroke, pulmonary embolus, major venous thrombosis or death from cardiovascular cause compared to placebo. Aspirin does not increase the incidence of major bleeding episodes compared to placebo.

Cytoreductive treatments such as hydroxyurea are used to treat high-risk polycythaemia vera.

Question 67 of 191

A 65-year-old male presents with a 2 year history of fatigue. Over the past year he has had progressive early satiety, vomiting and weight loss. On examination you note 10cm splenomegaly.

Investigation results are as follows:

Hb	84g/l	Na +	138 mmol/l	Bilirubin	22 µmol/l
Platelets	65 * 10 /l 9	K +	3.7 mmol/l	ALP	88 u/l
WBC	2.2 * 10 /l 9	Urea	4.5 mmol/l	ALT	22 u/l
Neuts	0.8 * 10 /l 9	Creatinine	68 µmol/l	γGT	96 u/l
Lymphs	0.4 * 10 /l 9	Albumin	28 g/l		

Blood film: Tear-drop poikilocytes

What is the most likely diagnosis?

A. Myelodysplasia due to bone marrow metastases
B. Chronic myeloid leukaemia
C. Acute myeloid leukaemia
D. Myelofibrosis
E. Megaloblastic anaemia

D. Myelofibrosis

Massive splenomegaly may early satiety and vomiting which can mimic gastric cancer

The blood results confirm pancytopenia with tear drop cells, suggestive of a primary marrow problem. Teardrop cells may be seen in the setting of marrow infiltration (by fibrosis, granulomatous inflammation, haematological or metastatic malignancy), splenic abnormalities, megaloblastic anaemia, and thalassemia.

In this case, the differential is clearly between gastric cancer (with bone marrow metastases resulting in myelodysplasia), and myelofibrosis. Early satiety and vomiting can be a feature of both gastric cancer, and massive splenomegaly. The presence of splenomegaly, and the duration of symptoms are more suggestive of myelofibrosis.

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A 56-year-old man presents to the clinic with a 1-week history of yellowing of his skin. He also complains of itching. A systematic inquiry was otherwise unremarkable. He drinks approximately 160 units of alcohol per week. Observations are within normal limits. On examination, there is palpable hepatosplenomegaly.

Blood results are as follows:

Hb	115 g/L	Male: (135-180)Female: (115 - 160)
Platelets	52 * 10 /L 9	(150 - 400)
WBC	4.8 * 10 /L 9	(4.0 - 11.0)
Reticulocytes	195 * 10 /L 9	(50 - 100)
Urea	2.8 mmol/L	(2.0 - 7.0)
Creatinine	42 µmol/L	(55 - 120)
LDH	520 units/L	(140 - 280)
Haptoglobins	<0.5 g/L	(0.5 - 2.2)
Triglycerides	4.2 mmol/L	(<2.3)

Prothrombin time (PT)	16 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	38 secs	(25-35 secs)
Fibrinogen	2.8 g/L	(2 - 4)
D-Dimer	360 ng/mL	(< 400)

Bilirubin	58 µmol/L	(3 - 17)
ALP	580 u/L	(30 - 100)
ALT	126 u/L	(3 - 40)
Î³GT	860 u/L	(8 - 60)
Albumin	28 g/L	(35 - 50)
Direct antiglobulin test (DAT)		Negative

What is the treatment of choice?

A. Abstinence from alcohol
B. Eculizumab
C. Intravenous immunoglobulin (IVIg)
D. Plasma exchange
E. Prednisolone

A. Abstinence from alcohol

Zieve syndrome usually resolves with abstinence from alcohol

The presence of anaemia with reticulocytosis is suggestive of bleeding or haemolysis. The suppressed haptoglobins, raised bilirubin, and raised LDH are highly suggestive of haemolytic anaemia. The causes of haemolytic anaemia are wide and include hereditary (e.g. membranopathies, enzymopathies, haemoglobinopathies), immunological (e.g. autoimmune haemolytic anaemia), infective (e.g. malaria), and microangiopathic haemolytic anaemias (e.g. TTP, DIC).

It is also important to note that the patient is thrombocytopenic. The cause of this most likely relates to cirrhosis with portal hypertension and splenomegaly, given the significant alcohol history and the presence of hepatosplenomegaly. However, it may also be due to a recent alcohol binge since ethanol is toxic to platelets and can cause transient thrombocytopenia which should resolve within a few days following the binge. However, in the context of haemolytic anaemia, it would also be important to consider microangiopathic haemolytic anaemias (e.g. TTP, HUS, HELLP) which can cause thrombocytopenia due to platelet consumption.

The patient is also coagulopathic which is most certainly related to cirrhosis with decreased production of liver-derived clotting factors.

Abstinence from alcohol is correct. The most likely diagnosis is Zieve's syndrome (ZS) which is characterised by a triad of cholestatic jaundice (high ALP/GGT/bilirubin), DAT-negative haemolytic anaemia, and hyperlipidaemia that develops secondary to alcohol-induced liver injury (most commonly following a binge). The patient fulfils all the criteria of this triad favouring this diagnosis. The treatment for Zieve's syndrome is abstinence from alcohol. Abstinence from alcohol would also be essential for preventing the progression of cirrhosis.

Eculizumab is incorrect. Eculizumab is a terminal complement inhibitor that specifically binds to the complement protein C5 with high affinity, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9. This drug is used to treat paroxysmal nocturnal haemoglobinuria (PNH). PNH presents with pancytopenia, intravascular haemolytic anaemia, and arterial/venous emboli. Although it remains within the differential diagnosis, the clinical and laboratory features are more in keeping with Zieve's syndrome.

Intravenous immunoglobulin (IVIg) is incorrect. IVIg can be used to treat autoimmunehaemolytic anaemia (AIHA). The patient clearly has haemolysis, however, the negative DAT makes AIHA an exceptionally unlikely diagnosis. Although DAT-negative haemolysis can occur it is exceedingly rare.

Plasma exchange is incorrect. Plasma exchange can be used to treat thrombotic thrombocytopenic purpura (TTP). Thrombotic thrombocytopenic purpura (TTP) is a microangiopathic haemolytic anaemia classically characterised by the pentad of fever, haemolytic anaemia, thrombocytopenia, and renal and neurologic dysfunction. Although it remains within the differential diagnosis,

the clinical and laboratory features are more in keeping with Zieve's syndrome.

Prednisolone is incorrect. Prednisolone can be used to treat autoimmune haemolytic anaemia (AIHA). The patient clearly has haemolysis, however, the negative DAT makes AIHA an exceptionally unlikely diagnosis. Steroids can also be used to treat alcoholic hepatitis, however, the liver function tests are predominantly cholestatic in this case.

Question 69 of 191

A 44-year-old woman presents to the clinic with bruising. This has progressively worsened over the past week. She has also been having frequent nose bleeds which self-terminate. Her past medical history includes rheumatoid arthritis for which she takes weekly methotrexate. She drinks approximately 64 units of alcohol per week.

Her observations are within normal limits. She is noted to have widespread petechia and purpura. On abdominal examination, there is palpable hepatosplenomegaly.

Blood results are as follows:

Hb	120 g/L	Male: (135-180)Female: (115 - 160)
Platelets	2 * 10 /L 9	(150 - 400)
WBC	8.0 * 10 /L 9	(4.0 - 11.0)
Neuts	6.0 * 10 /L 9	(2.0 - 7.0)
Urea	5.4 mmol/L	(2.0 - 7.0)
Creatinine	75 µmol/L	(55 - 120)
Bilirubin	16 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	146 u/L	(3 - 40)
Î³GT	582 u/L	(8 - 60)
Albumin	32 g/L	(35 - 50)
Prothrombin time (PT)	10 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	3.4 g/L	(2 - 4)
D-Dimer	360 ng/mL	(< 400)

What is the most likely cause of this patient's thrombocytopenia?

A. Disseminated intravascular coagulation (DIC)
B. Felty's syndrome
C. Immune thrombocytopenic purpura (ITP)
D. Portal hypertension
E. Thrombotic thrombocytopenic purpura (TTP)

C. Immune thrombocytopenic purpura (ITP)

ITP should be considered in the presence of symptoms that suggest isolated thrombocytopenia e.g. epistaxis, menorrhagia

The causes of thrombocytopenia are wide and include decreased production (e.g. bone marrow failure), increased consumption (e.g. MAHA), and sequestration (e.g. portal hypertension with splenomegaly).

Immune thrombocytopenic purpura (ITP) is correct. ITP is an acquired autoimmune disorder characterised by a low platelet count resulting from peripheral platelet destruction by autoantibodies. It can often be precipitated by malignancy, drugs, vaccinations, or infections. It is often commonly associated with other autoimmune disorders. A single-figure platelet count, with otherwise normal full blood count and a normal coagulation screen, is most likely a consequence of ITP.

Felty's syndrome is incorrect. Felty's syndrome is a rare, extra-articular manifestation of rheumatoid arthritis (RA), characterised by persistent, idiopathic neutropenia and, in some cases, splenomegaly. The absence of neutropenia makes this an unlikely diagnosis.

Disseminated intravascular coagulation (DIC) is incorrect. The normal coagulation profile excludes this diagnosis. DIC presents with prolonged PT, prolonged APTT, low fibrinogen and very high D-dimers.

Thrombotic thrombocytopenic purpura (TTP) is incorrect. Thrombotic thrombocytopenic purpura (TTP) is a microangiopathic haemolytic anaemia classically characterised by the pentad of fever, haemolytic anaemia, thrombocytopenia, and renal and neurologic dysfunction. The absence of any of the other criteria makes this an unlikely diagnosis.

Portal hypertension is incorrect. The patient certainly has features to suggest portal hypertension namely the significant alcohol history, deranged LFTs, and the presence of hepatosplenomegaly. Thrombocytopenia is a common complication in liver disease as a result of multiple factors, including splenic sequestration, reduced activity of the haematopoietic growth factor thrombopoietin, and bone marrow suppression by chronic hepatitis C virus infection. However, it is important to remember that the platelet count is rarely < 50 *10 /L in this setting. Therefore, although this may be a contributing factor in this clinical case, an alternative diagnosis should be considered, and indeed ITP is the most likely diagnosis.

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An 82-year-old man attends the clinic with a 6-month history of drenching night sweats and 10kg weight loss. He also complains of headaches and blurred vision. His observations are within normal limits. On examination, he has bulky bilateral cervical and inguinal lymphadenopathy.

Blood results are as follows:

Hb	115 g/L	Male: (135-180)Female: (115 - 160)
Platelets	185 * 10 /L 9	(150 - 400)
WBC	7.2 * 10 /L 9	(4.0 - 11.0)
Na +	135 mmol/L	(135 - 145)
K +	4.4 mmol/L	(3.5 - 5.0)
Urea	6.2 mmol/L	(2.0 - 7.0)
Creatinine	85 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Total protein	110 g/L	(60-80)

What is the most likely diagnosis?

A. Burkitt's lymphoma
B. Diffuse large B-cell lymphoma
C. Mantle cell lymphoma
D. Marginal zone lymphoma
E. Waldenstrom's macroglobulinaemia

E. Waldenstrom's macroglobulinaemia

Weight loss, raised total protein, hyperviscosity symptoms (headache, blurring) → ? Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is correct. The clinical features are suggestive of lymphoma (e.g. B symptoms and lymphadenopathy). The presence of headaches, and visual impairment, in the context of a raised total protein, is suggestive of hyperviscosity. Although formal serum electrophoresis and immunofixation are required to confirm and classify the paraprotein, it is usually IgM paraproteins that are implicated in hyperviscosity. This is because the IgM molecule is a massive pentameric structure. IgM paraproteins can be associated with many types of lymphoma, however, the classic cause is Waldenstrom's macroglobulinaemia, making this the most likely diagnosis.

Burkitt's lymphoma is incorrect. Burkitt's lymphoma is a highly aggressive high-grade lymphoma. It is the fastest-growing tumour seen in humans with a doubling time of between 24 and 48 hours. Thus the chronicity of the patient's symptoms makes this an exceptionally unlikely diagnosis.

Diffuse large B-cell lymphoma is incorrect. Diffuse large B cell lymphoma (DLBCL) is a highly aggressive high-grade lymphoma. Although not as rapidly growing as Burkitt's, the chronicity of the patient's symptoms makes this a less likely diagnosis.

Mantle cell lymphoma is incorrect. Although mantle cell lymphoma looks like a low-grade lymphoma under the microscope, it often behaviours more like a high-grade lymphoma (e.g. rapid growth). Although it can occasionally produce an IgM paraprotein, it is Waldenstrom's macroglobulinaemia which is more commonly associated with IgM paraproteins making this the more likely diagnosis.

Marginal zone lymphoma is incorrect. There are three types of marginal zone lymphomas (MZL): extranodal MZL of mucosa-associated lymphoid tissue (MALT or gastric GALT), splenic MZL, and nodal MZL. Although IgM paraproteins are occasionally associated with MZL, they are much closer associated with Waldenstrom's macroglobulinaemia making this the favoured diagnosis.

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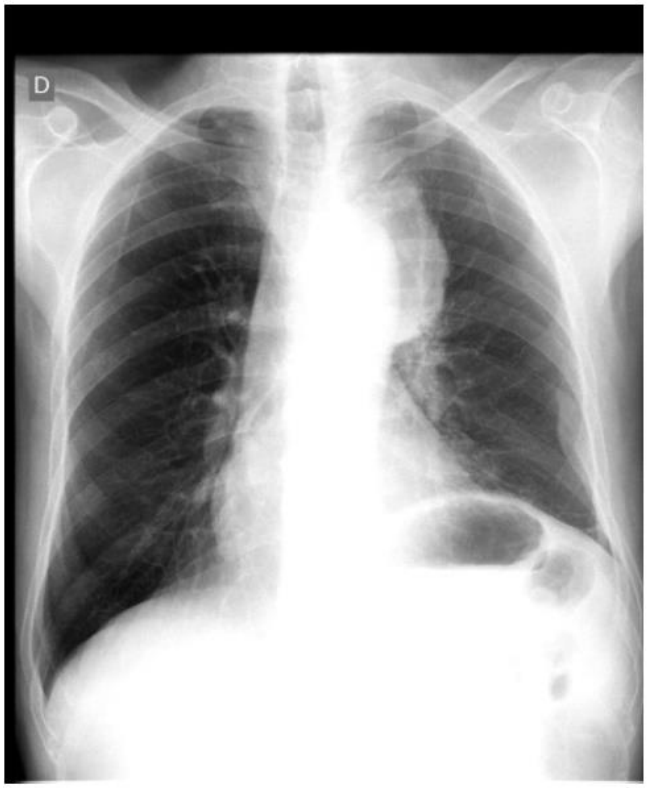
A 70-year-old man is investigated for dysphagia and chest pain. These symptoms have been getting progressively worse for the past 3 months and have not responded to a trial of a proton pump inhibitor. There is no history of weight loss or anorexia.

On examination you note a left-sided partial ptosis. The patient also complains of double vision when you are assessing eye movements. Sustained upward gaze exacerbates his ptosis.

A chest x-ray is requested:



What is the most likely diagnosis?

A. Lung cancer
B. Cardiac myxoma
C. Tuberculosis
D. Sarcodoisis
E. Thymoma

E. Thymoma

Anterior mediastinal mass + symptoms of myasthenia = thymoma

The chest x-ray shows is a partially delineated mediastinal mass (anterior mediastinum) with regular borders, bulging the left upper mediastinal contour. These findings are consistent with a thymoma.

The history is highly suggestive of myasthenia gravis which is seen in around a third of patients with a thymoma. Note how the ptosis worsened with sustained upward gaze, a demonstration of fatigability.

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A 53-year-old man presents to the emergency department with a rash and ulceration on his lower limbs. He has a past medical history of untreated hepatitis C virus. He is not on any regular medications. He is homeless. He is an intravenous drug user.

On examination, there is a purpuric rash on his lower limbs with ulceration of the digits. There is no clinical evidence of synovitis.

Blood tests:

Hb	121 g/L	Male: (135-180)Female: (115 - 160)
Platelets	422 * 10 /L	(150 - 400)
WBC	5.2 * 10 /L	(4.0 - 11.0)
Na	138 mmol/L	(135 - 145)
K	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	141 µmol/L	(55 - 120)
CRP	55 mg/L	(< 5)
Rheumatoid factor	654 IU/ml	(0-20)
Complement (C3)	0.81 g/L	(0.75 - 1.65)
Complement (C4)	.02 g/L	(0.16 to 0.48)
Antinuclear antibody	negative	(negative)
ESR	101 mm/Hr	(0-20)
IgA	10.2 g/L	(6.60 - 15.90)
IgG	24.1 g/L	(6-16)
IgM	4.2 g/L	(0.53-2.47)

Urinalysis:

Leucocytes	negative
Nitrites	negative
Blood	+++
Protein	++
Glucose	negative

What is the likely diagnosis?

A. Rheumatoid vasculitis
B. Systemic lupus erythematosus
C. Type I cryoglobulinaemia
D. Type II cryoglobulinaemia
E. Type III cryoglobulinaemia

D. Type II cryoglobulinaemia

Hepatitis C is associated with mixed (type II) cryoglobulinaemia

Type II cryoglobulinaemia is correct. This patient presents with a purpuric rash on the lower limbs with distal ulceration in association with hypocomplementaemia and a positive rheumatoid factor on a background of hepatitis C. This suggests a diagnosis of cryoglobulinaemia. Hepatitis C is associated with Type II cryoglobulinaemia. The haematoproteinuria and deranged renal function suggest glomerulonephritis. Rheumatoid factor may be very high in this condition.

Rheumatoid vasculitis is incorrect. This may cause a rash, ulceration and positive rheumatoid factor. However, it tends not to cause low complement and glomerulonephritis and is, therefore, less likely. Additionally, it tends to occur in longstanding rheumatoid, which is absent here.

Systemic lupus erythematosus is incorrect. This can be associated with rash, low complement, rheumatoid factor and ulceration. However, a negative ANA essentially excludes the diagnosis.

Type I cryoglobulinaemia is incorrect. This form of cryoglobulinaemia is typically associated with a monoclonal IgM or IgG rather than a polyclonal picture. It is associated with multiple myeloma and Waldenstrom's macroglobulinaemia.

Type III cryoglobulinaemia is incorrect. This type of cryoglobulinaemia is typically associated with rheumatoid arthritis and Sjogren's rather than hepatitis C. The absence of joint symptoms and the negative ANA make rheumatoid arthritis and Sjogren's unlikely.

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A 19-year-old African male was referred by his GP to the medical assessment unit with a complaint of dark coloured urine, abdominal pain and jaundice. He does not have any other co-morbidities and there is no family history of haemolytic anaemias. He recently tried a new Mediterranean diet containing fava beans. On examination, there is moderate splenomegaly.

Hb	70 g/l	Na +	137 mmol/l	Bilirubin	107 µmol/l
Platelets	280 * 10 /l 9	K +	4.3 mmol/l	ALP	98 u/l
WBC	8.7* 10 /l 9	Urea	5.6 mmol/l	ALT	25 u/l
Neuts	5.6 * 10 /l 9	Creatinine	77 µmol/l	γGT	37 u/l
Lymphs	1.3 * 10 /l 9	Albumin	35 g/l		
Eosin	0.9 * 10 /l9				

Serum haptoglobin was undetectable, and serum lactate dehydrogenase (LDH) was 1987 units/l. Peripheral blood film showed Heinz bodies. A direct Coombe's test was negative. G6PD levels return as normal.

What investigation should be performed next to confirm the diagnosis?

A. Repeat G6PD level immediately as the first specimen may have been inadequate
B. Ultrasound abdomen
C. Hepatitis serology
D. Bone marrow examination
E. G6PD analysis in few weeks when symptoms improved

E. G6PD analysis in few weeks when symptoms improved

G6PD deficiency: G6PD level may be normal during an acute haemolytic episode

G6PD testing should be performed when patients are in remission as the result may be falsely negative during acute haemolysis. The reason for this is that during an acute haemolytic episode, older erythrocytes with low G6PD levels are destroyed and there is a compensatory increase in immature erythrocytes and reticulocytes that have increased G6PD levels. Although ultrasound abdomen may be useful in assessing for splenomegaly and gallstones in this patient, it's not diagnostic of G6PD deficiency.

Hepatitis serology is more useful in the setting of jaundice secondary to hepatobiliary disease. Bone marrow examination is not an investigation of choice in G6PD deficiency.

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A 72-year-old man is brought into the emergency department following a fall. He was found by his daughter unresponsive on the floor after hearing a loud bang. His daughter tells you that he has been more unsteady on his feet for the last few days and is recovering from a urinary tract infection. There is a past medical

history of benign prostatic hyperplasia and atrial fibrillation for which he takes tamsulosin, finasteride and rivaroxaban.

On examination, he is drowsy with a GCS of 12 (E3V4M5). He has a heart rate of 85bpm and blood pressure of 210/118mmHg. On auscultation, his chest is clear with normal heart sounds. Oxygen saturations are 90% on air. There is a deep laceration over the left side of his forehead which is oozing blood and there is bruising down the left side of his body. Pupils are equal and reactive to light.

CT Head: Evidence of a moderate intracranial haemorrhage in the left frontal lobe. There is no evidence of a mass effect.

What is the most appropriate next step in the management of this patient?

A. Andexanet alfa
B. Cryoprecipitate
C. Dexamethasone
D. Idarucizumab
E. Protamine

A. Andexanet alfa

Rivaroxaban and apixaban can be reversed by andexanet alfa

Important for me Less im This patient has had a traumatic intracranial haemorrhage. Initial treatment should be to maintain a patent airway and attempt to stop the bleeding in order to prevent raised intracranial pressures. With patients taking anticoagulant therapy, actions should be taken to reverse their action. Andexanet alfa is a recombinant form of factor Xa which binds specifically to apixaban or rivaroxaban to reverse their anticoagulant effects.

Cryoprecipitate is derived from fresh frozen plasma and contains factor VIII, factor XIII, fibrinogen, vWF and fibronectin. It is used to treat fibrinogen deficiency in cases of disseminated intravascular coagulation, trauma, invasive procedures or haemorrhage. It is more commonly used to treat an intracranial haemorrhage secondary to tissue plasminogen activator use for an acute ischaemic stroke.

Dexamethasone can be given in the case of increased intracranial pressure, which can be secondary to intracranial haemorrhage and subsequent mass effect. However, the current investigations do not show evidence of cerebral oedema or midline shift and therefore dexamethasone is not the next initial treatment to be given.

Idarucizumab is a specific reversal agent for dabigatran. As this patient is not taking dabigatran therapy, the use of idarucizumab is not indicated.

Protamine is used in the reversal of heparin. As this patient is not taking heparin therapy, the use of protamine is not indicated.

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A 24-year-old female presents to her GP with a 2 month history of tiredness. On further questioning she admits she has also been experiencing pain in the centre of her chest and in the lymph nodes in her neck when drinking alcohol.

What is the likely underlying cause?

A. Hodgkin's lymphoma
B. Somatisation disorder
C. GORD (gastro-oesophageal reflux disease)
D. Hiatus hernia
E. Pancreatitis

A. Hodgkin's lymphoma

Lymph node pain when drinking alcohol is very specific for Hodgkin's lymphoma (although it occurs rarely)

Lymph node pain when drinking alcohol is very specific for Hodgkin's lymphoma. It is however a rare symptoms and most patients do not experience it.

None of the other conditions mentioned cause pain in lymph nodes

Question 76 of 191

You are the medical registrar on call. The surgical registrar contacts you for a patient he has just seen in clinic who requires an elective cholecystectomy. The patient is a 65-year-old woman who has atrial fibrillation for which she takes rivaroxaban. The patient is otherwise well. The bloods performed in clinic that day are as follows:

Hb	131 g/l
Platelets	352 * 10 /l9
WBC	5.5 * 10 /l9
INR	1.5
Na +	137 mmol/l
K +	3.6 mmol/l
Urea	3.2 mmol/l
Creatinine	67 µmol/l

The surgical registrar would like to know how long the patient should omit their anticoagulation before the procedure?

A. 1 day
B. 2 days
C. 3 days
D. 5 days
E. 7 days

A. 1 day

The new oral anticoagulant drugs (NOACs) are being used increasingly in patients who require anticoagulation. They have the advantage of once or twice daily dosing regimes, oral formulation and do not require therapeutic monitoring like warfarin. They are particularly useful in patients that may have issues with warfarin compliance or those with erratic international normalised ratio (INR) readings. NOACs have been shown to convey equivalent efficacy to warfarin in most contexts the main exception being anticoagulation in patients with prosthetic heart valves where NOACs were not as effective as warfarin.

Rivaroxaban is one of the most commonly used agents. It acts as a direct factor Xa inhibitor. It is absorbed from the gut and has maximum factor Xa inhibition four hours post dose. It is indicated for anticoagulation in atrial fibrillation and in the treatment of venous thromboembolism. It has a half-life of 7-9 hours and is metabolised in the liver. Factor Xa levels do not return to normal for just over 24 hours so once daily dosing is appropriate.

The following table outlines how long anticoagulants need to be withheld before surgery:

Drug	Duration to withhold before procedure
Dabigatran	1-2 days with creatinine clearance >50ml/min
Rivaroxaban	1 day if creatinine clearance >90 ml/min
Apixaban	1-2 days if creatinine clearance >60
Fondaparinux	36-48 hours
LMWH	12 hrs for prophylactic dose, 24 hours for therapeutic dose
Warfarin	1-8 days, check INR
UFH	IV 4-6 hrs, SC 12-24 hrs

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A 45-year-old worker on demolition sites comes to the Emergency department for review. He has suffered increasing tiredness, lethargy, headache, and abdominal pains over the past 2 months. On examination he is hypertensive with a blood pressure of 155/90 mmHg, his pulse is 85 beats per minute and regular. He looks pale.

Investigations

Hb	97 g/l
MCV	78 fl
Platelets	175 * 10 /l9
WBC	6.2 * 10 /l9
Lead	5 µmol/l

Blood film reveals basophilic stippling

Which of the following is the most appropriate initial intervention?

A. Activated charcoal
B. Disodium EDTA
C. DMSA
D. Haemodialysis
E. Vitamin C

C. DMSA

DMSA is an oral chelation therapy that can be used for chronic lead poisoning, the diagnosis here. A lead level above 3.4 µmol/l indicates significant occupational exposure and that the patient should be withdrawn from work. 500mg twice per day is a usual initial therapeutic dose.

Given his lead exposure represents chronic exposure, there is no role for activated charcoal. Disodium EDTA is used in the management of acute lead poisoning and is given intravenously. Human trials of vitamin C with respect to treatment of lead toxicity are so far equivocal, and there is no role for haemodialysis in chronic lead poisoning.

Question 78 of 191

A 65-year-old man is seen in the haematology clinic for review of test results. He has been fatigued for the last three months and has experienced night sweats. On examination he is pale with a palpable spleen 4cm below the costal margin, mildly tender on palpation. His only other past medical history is of osteoarthritis.

His results are as follows:

Hb	89 g/l	Na +	140 mmol/l
Platelets	205 * 10 /l 9	K +	4.0 mmol/l
WBC	5 * 10 /l 9	Urea	5.8 mmol/l
Neuts	3.6 * 10 /l 9	Creatinine	72 µmol/l
Lymphs	1.2 * 10 /l 9	CRP	3 mg/l

Blood film: Anisocytosis with mild hypochromia. Tear drop cells. CT chest/abdomen/pelvis: Splenic enlargement. No suspicious mass lesions seen. 1cm simple right renal cyst. No lymphadenopathy.

Bone marrow biopsy: Fibrosis

Which initial therapy should be used to treat this gentleman?

A. Chlorambucil
B. Fludarabine
C. Hydroxycarbamide
D. Interferon alpha
E. Lenalidomide

C. Hydroxycarbamide

This gentleman has myelofibrosis as evidenced by bone marrow fibrosis, tear drop cells on blood film and constitutional symptoms. He has symptomatic splenomegaly and anaemia. First line treatment for this would be hydroxycarbamide.

Chlorambucil is used in chronic lymphocytic leukaemia and non-Hodgkin lymphoma. Fludarabine is used to treat acute myeloid leukaemia. Interferon alpha is used for myelosuppression in myelofibrosis in the presence of thrombocytosis or leucocytosis. Lenalidomide is used in the treatment of multiple myeloma

Question 79 of 191

A 30-year-old lady presents with shortness of breath and facial flushing. She had been to a restaurant that evening and noticed the symptoms when rushing home. She also had itchy skin and tingling lips. On examination she was tachycardic with a wheeze. She had no history of food allergies and reported eating lasagne for dinner alongside a glass of wine.

What is the most likely diagnosis?

A. Acute asthma attack
B. Carcinoid syndrome
C. Exercise induced wheat angioedema
D. Shellfish anaphylaxis
E. Thyrotoxicosis

C. Exercise induced wheat angioedema

Exercised induced anaphylaxis is now well described and is most associated with wheat ingestion. The clinical manifestations usually occur around 10 minutes after exercise and follow a sequence of pruritus, widespread urticaria and then subsequently respiratory distress and vascular collapse. The condition usually resolves on stopping exercise and is managed in the same manner as anaphylaxis. The patients can usually eat the causative food without problems so long as they do not exercise afterwards. The physiology of the condition remains slightly unknown, but it may be related to endorphin release during exercise. The endocrines cause excessive histamine release from mast cells in susceptible individuals.

The tingling lips and facial flushing are not in keeping with an asthma attack and there is no history of shellfish consumption. Thyrotoxicosis could explain some of the symptoms but not the wheeze. Carcinoid syndrome can cause episodes of flushing, shortness of breath and tachycardia and thus represents a plausible option, especially as exercise, food and stress can trigger these episodes. However these patients often have diarrhoea and abdominal symptoms alongside their other symptoms.

Question 80 of 191

A 54-year-old man presents to the emergency department with shortness of breath. He has a history of heart failure and takes ramipril, bisoprolol, eplerenone and isosorbide mononitrate.

Observations are as follows: heart rate 135 beats per minute, respiratory rate 26 breaths per minute, blood pressure 135/82 mmHg, temperature 37.4 ºC, and SpO2 92%. His chest is clear on auscultation.

The doctors initiate the patient on 15L O2 via a non-rebreather mask. Blood gas analysis results are as follows:

pH	7.24	(7.35 - 7.45)
PaO2	72.4 kPa	(10.3 - 13.3 kPa)
PaCO2	2.9 kPa	(4.7 - 6 kPa)
HCO3	16 mmol/L	(22 - 28 mmol/L)
SaO2	44%	(94 - 98%)
Lactate	3.4 mmol/L	(<1.0)

What is the most likely diagnosis?

A. Acquired methaemoglobinaemia
B. Carboxyhaemoglobinaemia
C. Congenital methaemoglobinaemia
D. Cyanide poisoning
E. Pulmonary embolism

A. Acquired methaemoglobinaemia

Nitrates, including recreational nitrates such as amyl nitrite ('poppers') may cause methaemoglobinaemia

The striking feature, in this case, is the significant discrepancy between the PaO2 and SaO2 on arterial blood gas analysis. Given the patient is on 15L O2, the PaO2 is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. There are various formulas for predicting the expected PaO2 for any given inspired O2 concentration. The Advanced Life Support (ALS) guidelines suggest that the PaO2 for any given inspired concentration should be approximately 10 less than the inspired concentration (%). For example, in this case, 15L O2 is equivalent to approximately 80-85% so we would expect the PaO2 to be around 70 kPa.

However, it is important to note that the SaO2 (oxygen saturation of haemoglobin) is markedly low at 44% indicating impaired oxygen binding to haemoglobin. It is also important to note that the peripheral SpO2 is 92% which is clearly discrepant with the SaO2. The two main causes of this picture are methaemoglobinaemia and carboxyhaemoglobinaemia. Because standard pulse oximeters are not capable of differentiating between different forms of bound haemoglobin, the SpO2 is usually falsely high in these conditions.

Tissue hypoxia can be a consequence of 4 main causes:

1. Hypoxaemia (low PaO2 due to poor gas exchange at the alveoli)
2. Toxic haemoglobin (low SaO2 due to methaemoglobinaemia or carboxyhaemoglobinaemia)
3. Perfusional (e.g. shock, or localised causes such as compartment syndrome or bowel ischaemia)
4. Severe anaemia

Regardless of the cause, tissue hypoxia will result in lactic acidosis. Therefore, in patients with lactic acidosis, all the aforementioned causes should be considered. The patient in this case most certainly has lactic acidosis as a consequence of toxic haemoglobin-induced tissue hypoxia. He is acidotic with low serum bicarbonate since this acts as a buffer for lactic acid.

Acquired methaemoglobinaemia is the correct answer. As discussed above, the biochemical results are suggestive of toxic haemoglobin. The history of isosorbide mononitrate use favours the diagnosis of acquired methaemoglobinaemia. Nitrate-containing drugs are commonly implicated in this condition.

Carboxyhaemoglobinaemia is incorrect. Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the history of nitrate exposure favours the diagnosis of methaemoglobinaemia.

Congenital methaemoglobinaemia is incorrect. Although this remains within the differential diagnosis, the absence of previous episodes and the presence of a known risk factor (e.g. nitrate exposure) favours the acquired form.

Cyanide poisoning is incorrect. Cyanide binds the ferric (Fe3+) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO2 as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this clinical case to suggest that this is the case.

Pulmonary embolism is incorrect. As stated above, the blood gas analysis confirms hypoxaemia as a consequence of toxic haemoglobin rather than poor gas exchange at the level of the alveolar. Therefore a pulmonary embolism is a less likely diagnosis.

Question 81 of 191

A 75-year-old man presents to the emergency department with a reduced level of consciousness after a recent fall and head injury. He has a past medical history of atrial fibrillation. His medications include apixaban and bisoprolol.

On examination, his Glasgow coma scale is 12/15 (E 3 V4 M5). There is evidence of an external head injury with bruising and laceration in the right occipital area.

An urgent CT head is arranged, which demonstrates a large right-sided subdural haematoma.

What is the most appropriate medication to administer?

A. Andexanet alfa
B. Fresh frozen plasma
C. Vitamin K
D. Prothrombin complex
E. Idarucizumab

A. Andexanet alfa

Rivaroxaban and apixaban can be reversed by andexanet alfa

Andexanet alfa is the correct answer. The patient has sustained a traumatic subdural haematoma. Clinically he has a low GCS. The method of anticoagulation needs to be reversed. The most appropriate reversal agent for apixaban is andexanet alfa.

Vitamin K is incorrect. This can be used as a reversal agent for warfarin. It is not the most appropriate agent to use given this patient's method of anticoagulation.

Fresh frozen plasma is incorrect. This is mainly used to replace coagulation factors in cases of excessive bleeding or in those with abnormal coagulation. It is not the most appropriate reversal agent available to choose in this case.

Prothrombin complex is incorrect. This can be used to rapidly reverse the effects of warfarin in those patients that are bleeding. It is under investigation currently to see if it is effective in reversing agents such as apixaban Idarucizumab is incorrect. This is a monoclonal antibody that can reverse the effects of dabigatran

Question 82 of 191

You are looking after a 35-year-old man who is in the oncology day unit receiving his second round of chemotherapy for a low grade non-Hodgkin's lymphoma. His lymphoma is confined to two lymph node groups in his anterior cervical chain and right inguinal region. In total there are 6 nodes with the largest being 4cm in size. He had no issues during his first round of chemotherapy apart from some nausea a week afterwards. He has no other medical problems and is on no other medications. His bloods pre-chemotherapy are as shown below:

Na +	137 mmol/l
K +	3.8 mmol/l
Urea	2.8 mmol/l
Creatinine	55 µmol/l
Corrected Calcium	2.39 µmol/l
Phosphate	1.05 µmol/l

What regimen would be most appropriate for prevention of tumour lysis syndrome in his case?

A. Allopurinol (200mg BD)
B. Fluids and allopurinol (200mg BD)
C. Fluids and rasburicase (0.2mg/kg)
D. Reduced dose chemotherapy
E. Fluids, allopurinol (200mg BD) and rasburicase (0.2mg/kg)

B. Fluids and allopurinol (200mg BD)

The British Society of Haematology suggest that patients undergoing chemotherapy can be categorised into three different risk groups for tumour lysis syndrome. While you are not required to know how to do this in detail it would be important clinically to be able to recognise factors that put people at increased risk:

- High tumour burden
- High grade tumours with rapid cell turnover
- Pre-existing renal impairment or renal involvement by the tumour Increased age
- Treatment with highly active, cell-cycle specific agents
- Concomitant use of drugs that increase uric acid levels (the list is available on the guidance)

Risk Group	Prophylaxis
Low Risk	Adequate hydration (consider IV fluids and allopurinol prophylaxis)
Intermediate Risk	Allopurinol (7 days) and IV fluids
High Risk	Rasburicase and IV fluids (consider low dose chemotherapy)

This patient has no high risk features in his history and is therefore considered low risk, so the closest answer is fluids and allopurinol.

It is important to know that allopurinol and rasburicase should not be used together, as allopurinol reduces the effectiveness of rasburicase. Allopurinol reduces the production of urate, allowing elimination of upstream compounds, which are more water soluble and thus more easy to excrete through the kidneys. Rasburicase, on the other hand, converts urate into more easily excreted downstream compounds.

In addition rasburicase cannot be given to patients with G6PD as it can precipitate haemolysis.

Question 83 of 191

A 24-year-old man is brought into the resuscitation room. They were struggling to walk across the emergency department reception area due to severe dyspnoea.

They admit to inhaling some substances at a party earlier in the evening but cannot recall what it was.

On examination, they have blue-tinged peripheries with blue lips and tip of nose but appear relatively undistressed. Their observations show oxygen saturations of 90% on 6 litres of oxygen and a heart rate of 120 beats per minute.

An arterial blood gas is taken while they are on 6 litres of oxygen. The results are below.

pH	7.40	(7.35-7.45)
paO2	18	(11-13)
paCO2	4.6	(4.5-6)
methaemoglobin	38%	(1-3%)

What is the most likely substance that they have ingested?

A. Amyl nitrite
B. Glyceryl trinitrate
C. Sodium nitroprusside
D. Aniline dye
E. Dapsone

A. Amyl nitrite

Nitrates, including recreational nitrates such as amyl nitrite ('poppers') may cause methaemoglobinaemia

The answer is amyl nitrite otherwise known as 'poppers' which is a drug of abuse. It induces a short lived euphoric high but can result in methaemoglobinaemia. The other answers all cause methaemoglobinaemia but are unlikely to be used in the above context.

Question 84 of 191

You are called to see a 55-year-old gentleman who is having a blood transfusion for symptomatic anaemia secondary to colon cancer. The nurses have been doing regular observations as documented below.

10am:

Baseline observations prior to blood transfusion

- Respiratory rate 20 breaths/min
- Saturations 96% on air
- Temperature 37.5 ºc
- Blood pressure 145/78 mmHg
- Heart rate 74 beats/min

10:15 am: repeat observations after 15 mins of transfusion

- Respiratory rate 19 breaths/min
- Saturations 97% on air
- Temperature 38.2 ºc
- Blood pressure 150/80 mmHg
- Heart rate 72 beats/min

The nurses have already stopped the blood transfusion by the time you arrive to see the patient. On questioning the patient he feels well with no complaints of pain, itch or rashes. On examination his heart sounds are pure and chest is clear. He has no previous documented reactions to blood transfusions although the patient informs you he is allergic to penicillin.

What instructions do you give the nurses?

A. Take blood cultures and commence antibiotics
B. Dispose of the remaining blood in the bag
C. Restart the blood transfusion after giving the patient paracetemol
D. Take blood cultures, repeat chest x ray and perform urinalysis
E. Restart the blood transfusion an hour after giving the patient paracetemol

C. Restart the blood transfusion after giving the patient paracetemol

Blood transfusion reaction are common and can be serious. This patient is well and has no clinical evidence of haemodynamic compromise. He has an isolated pyrexia which is likely to be secondary to commencement of the blood transfusion. After confirming this his blood transfusion should be restarted as soon as possible and paracetemol given for symptomatic relief. Disposal of the blood should be considered if a serious adverse reaction occurs. Septic screen and antibiotics should be considered if any underlying infection is suspected. Blood transfusion should be completed within 4 hours and waiting an hour prior to restarting is a waste of valuable time.

Question 85 of 191

A 55-year-old lady presents to her general practitioner with a painful rash on her breasts. The rash has developed over the last 24 hours and although initially diffuse and red is now well demarcated and a much darker red. She was started on warfarin five days ago for a deep vein thrombosis diagnosed on ultrasound doppler. She has a past medical history of hypothyroidism, type two diabetes mellitus, thromboembolism and obesity. She remembers having been on warfarin at least once before for previous deep vein thrombosis but does not remember ever having had this rash. Her blood tests today are as follows.

Prothrombin time	21.4 seconds
INR	2.1 ratio

What is the most likely diagnosis?

A. Protein S deficiency
B. Idiosyncratic drug reaction
C. Stevens Johnson syndrome
D. Warfarin toxicity
E. Protein C deficiency

E. Protein C deficiency

Warfarin-induced skin necrosis is a symptom of the hypercoagulable state that can be seen in the first week of warfarin therapy. This is explained by the fact that warfarin inhibits both procoagulant factors (2, 7, 9, 10) as well as anti-coagulant factors (protein C). Protein C has the shortest half-life and therefore there is a short period of time during the initiation of warfarin therapy where the patient is hypercoagulable despite a therapeutic INR. Warfarin-induced skin necrosis is more likely to occur in patients with pre-existing protein C deficiency, which is a rare congenital condition associated with recurrent venous thromboembolic disease.

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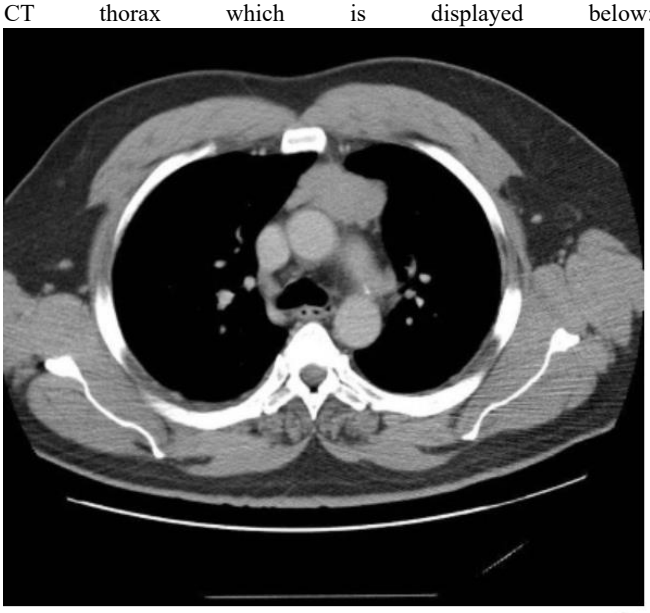
A 41-year-old woman presents to her general practitioner with a three-month history of shortness of breath and cough. Her symptoms have been progressive and she is otherwise asymptomatic. She has no relevant medical comorbidities but a 30 pack-year smoking history.

Examination of the respiratory systems is unremarkable. She has a CT thorax which is displayed below:



What is the most likely cause for this woman's symptoms?

A. Bronchial cancer

B. Chronic pulmonary emboli
C. Lung fibrosis
D. Thymoma
E. Thyroid cancer

D. Thymoma

This woman's CT scan demonstrates a large mass representing a thymoma in the anterior mediastinum. Thymomas can commonly cause shortness of breath and cough, as well as retrosternal chest pain, dysphagia, and vocal changes. Although bronchial cancer could cause this woman's symptoms, there is no evidence of this pathology on the CT and therefore this answer is incorrect.

There is no evidence on this CT scan of a pulmonary embolus despite this not being a pulmonary angiogram. As the scan does identify a thymoma, chronic pulmonary emboli are therefore less likely and incorrect.

Although not a high-resolution scan, there is no evidence of fibrosis within the lung fields and therefore this answer is incorrect.

The anterior mediastinal mass shown on this CT scan is too inferior to be a thyroid cancer which would typically present as a lump in the neck. Therefore the diagnosis of thymoma is more likely and thyroid cancer is incorrect.

Question 87 of 191

A 64-year-old woman presents to her general practitioner with a one-day history of swollen left leg associated with pain. She has a past medical history of heart failure and hypertension and takes bisoprolol, ramipril, amlodipine, and furosemide. She is significantly limited in her mobility.

On examination, the left calf is red and 4cm larger than the right. There is tenderness over the deep venous system. There is bilateral, symmetrical pedal oedema. The left thigh is unremarkable.

2-level DVT Wells test

Criteria	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

What is the most appropriate next step?

A. CT pulmonary angiogram
B. D-dimer
C. Inferior vena cava filter
D. Lower limb venous ultrasound
E. VQ scan

D. Lower limb venous ultrasound

This woman has a 2-level Wells' score of 2 (calf swelling, tenderness over the deep venous system) for deep vein thrombosis (DVT). NICE guidance states that a score of 2 or above should be investigated by **lower limb venous ultrasound** rather than high sensitivity d-dimer testing. **CT pulmonary angiography** (CTPA) could be considered to check for a pulmonary embolus (PE) once a DVT is confirmed however this is not indicated at this stage.

High-sensitivity **d-dimer** testing is the first-line investigation for patients who have a 2-level Wells' score of less than 2. As this patient scores 2, a lower limb ultrasound should be performed and therefore this is an incorrect answer.

An **inferior vena cava filter** is a treatment for DVT, particularly in cases where anticoagulation is not an option. As a DVT has not been confirmed, this would not be the most appropriate next step.

A **VQ scan** is an alternative imaging modality to CTPA for PE however as previously discussed, prior to confirmation of a DVT and with no clinical indication, this test would not be indicated at this stage.

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A 19-year-old man presents to your clinic. For as long as he can remember, he has had a dusky discolouration that is not in keeping with the skin colour of any of his relatives, and he feels that it is becoming gradually duskier with time. He tells you that. The only medication he is taking is oral isotretinoin, for acne, which he has been taking on-and-off for four years. Auscultation of his chest was unremarkable. Oxygen saturation by pulse oximetry showed saturation of 91% and an arterial blood gas was done which showed a pO2 of 10.6kPa, FO2Hb of 65% and metHb of 30%.

What is the most appropriate treatment for this man?

A. Ascorbic acid
B. Corticosteroids
C. Methylene blue
D. Nocturnal CPAP
E. Vitamin A

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A 24 year-old medical student of Italian extraction returns from elective in India. One week after his return he presents with fever, headache, and myalgia.

Investigations are as follows:

Hb	10.1 g/dl
MCV	101.2 fl
Platelets	43 x10^9/l
WCC	6.1 x10^9/l
Na	134mmol/l
K	4.6 mmol/l
Urea	3.8 mmol/l
Creatinine	80 mol/l

ALT	44 IU/l
ALP	78 IU/l
Bilirubin	33 mol/l
Albumin	38 g/l
Thick and thin blood films	Plasmodium ovale parasites with red cells

What other blood test will be essential for the management of this condition?

A. Coomb's test
B. G6PD enzyme assay
C. Chloroquine resistance test
D. Ham's test
E. Reticuloctye count

B. G6PD enzyme assay

Primaquine can precipitate haemolysis in individuals with G6PD (glucose-6-phosphate dehydrogenase) deficiency. G6PD activity should be tested before commencing treatment. If deficient, expert advice should be sought.

Coomb's test, also known as the direct antiglobulin test (DAT), detects antibody bound to the surface of red cells and is a test for autoimmune haemolytic anaemia. A variable degree of haemolysis occurs in malaria, but is not typically autoimmune. Rather it is due predominantly to destruction of infected red cells during parasite replication and breakdown in the spleen.

Chloroquine is the first-line treatment for non-falciparum malaria. Chloroquine resistance in *Plasmodium ovale* and *malariae* is extremely rare, but has been reported for vivax. Chloroquine is inadequate for the treatment of falciparum malaria as resistance is widespread.

Ham's test was previously used for the diagnosis of paroxysmal nocturnal haemoglobinuria, a condition which causes intravascular haemolysis.

Reticulocytes are red cell precursors, which are prematurely released from the marrow in response to haemolysis. Their large size accounts for the macrocytosis which often accompanies haemolytic anaemia. An elevated reticulocyte count is an appropriate response to haemolysis in the presence of an adequately functioning bone marrow.

Question 90 of 191

A 61-year-old woman comes for review. Around one year ago she finished a 6 month course of warfarin after being diagnosed with an unprovoked, proximal deep vein thrombosis. For the past few weeks she has been experiencing 'heaviness' and 'aching' in the the same leg. This is associated with an itch and some swelling, although this seems to go down each night. Past medical history of note includes osteoarthritis and type 2 diabetes mellitus.

On examination prominent varicose veins are seen on the affected leg with some brown discolouration of the skin above the medial malleolus. There is no difference in the circumference of the calves. Her temperature is 36.9ºC, pulse 78/min and blood pressure 108/82 mmHg.

What is the most likely diagnosis?

A. Recurrence of deep vein thrombosis
B. Post-thrombotic syndrome
C. Cellulitis
D. Ruptured Baker's cyst
E. Necrobiosis lipoidica

B. Post-thrombotic syndrome

Post-thrombotic syndrome is the correct diagnosis. This chronic condition develops in approximately 20-50% of patients following deep vein thrombosis (DVT) and typically presents with symptoms including leg heaviness, aching, pruritis, and oedema that improves with elevation (such as overnight). The presence of varicose veins and skin changes (particularly brown discolouration or hyperpigmentation) above the medial malleolus are classical signs. The pathophysiology involves damage to venous valves during the initial DVT, leading to chronic venous insufficiency.

Recurrence of DVT would be less likely in this case. While unprovoked DVT does carry a higher risk of recurrence, the clinical features are different. Acute DVT typically presents with more significant unilateral leg swelling, warmth, and tenderness. The improvement in symptoms overnight and chronic skin changes point away from acute DVT.

Cellulitis can be excluded based on the presentation. Cellulitis typically presents with acute onset erythema, warmth, tenderness, and often systemic symptoms such as fever. The patient's normal temperature and chronic nature of symptoms make this diagnosis unlikely.

Ruptured Baker's cyst typically presents with acute calf pain and swelling, often following activity. The pain is usually localised to the popliteal fossa and posterior calf. The chronic nature of symptoms and venous changes make this diagnosis unlikely.

Necrobiosis lipoidica is a rare condition associated with diabetes mellitus that presents with welldemarcated, waxy, atrophic plaques, typically on the anterior shin. While this patient does have diabetes, her presentation with venous symptoms and characteristic post-thrombotic changes makes necrobiosis lipoidica an unlikely diagnosis.

Question 91 of 191

A 62-year-old gentleman with a background of Rheumatoid Arthritis, on maintenance sulfasalazine, is referred to the medical take from his GP with severe unremitting flu-like symptoms and deranged blood tests.

On examination, his temperature is 38.3 degrees celsius, heart rate 104bpm, respiratory rate 31/min and oxygen saturations 92% on room air.

His blood test reveals the following:

Hb	82 g/l
Platelets	52 * 10 /l9
WBC	18 * 10 /l9
Ferritin	50,000ng/ml
EBV Monospot test +ve	

He is initially treated as neutropaenic sepsis, with broad spectrum antimicrobials, and transferred to the intensive care unit for organ support. Unfortunately, he does not make any improvement. He is

then seen by haematology who organise a bone marrow aspirate, revealing haemophagocytosis

. What is the most likely underlying diagnosis?

A. Macrophage activation syndrome
B. Drug-induced pancytopaenia
C. Atypical infection
D. Parvovirus infection
E. Felty syndrome

A. Macrophage activation syndrome

Macrophage activation syndrome is a condition characterised by excessive immune stimulation and cytokine storm in a rheumatological patient with an intercurrent EBV infection.

There is no suggestion in the question that there is a parvovirus infection and Felty syndrome would be characterised by a neutropaenia and splenomegaly. Drug-induced pancytopaenia and atypical infections would not commonly show haemophagocytosis in the bone marrow.

Question 92 of 191

A 45-year-old woman is reviewed shortly after being diagnosed with having a pulmonary embolism. Around two weeks ago she was admitted with a severe community-acquired pneumonia which resulted in her being ventilated and admitted to ITU. She responded well to intravenous antibiotics but shortly before discharge became more short-of-breath again. A CTPA was requested which showed a pulmonary embolism. She is started immediately on dalteparin.

What is the most appropriate next step?

A. Stop dalteparin. Start a direct oral anticoagulant for 6 weeks
B. Stop dalteparin. Start a direct oral anticoagulant for 3 months
C. Stop dalteparin. Start a direct oral anticoagulant for 6 months
D. Keep on dalteparin for 6 weeks
E. Keep on dalteparin for 3 months

B. Stop dalteparin. Start a direct oral anticoagulant for 3 months

As this patient developed a pulmonary embolism secondary to something (in this case severe illness with associated immobility) an anticoagulation period of 3 months is generally recommended

Question 93 of 191

A 68-year-old gentleman with known chronic lymphocytic leukaemia (CLL) is reviewed in the Haematology Clinic.

He is normally an active gentleman who enjoys playing golf 3 times per week, but he complains that he has been feeling increasingly fatigued since his last appointment 6 months previously. He states that he has not been able to play golf for several weeks and his wife tells you that he has started napping during the afternoons. His past medical history is otherwise unremarkable and he takes no regular medications.

Examination reveals a tired gentleman with marked axillary and inguinal lymphadenopathy. His abdomen is soft with mild upper abdominal tenderness. A liver edge is palpable 3cm below the costal margin and his spleen is markedly enlarged.

His full blood count today is as follows:

Hb	114 g/l
Platelets	173 * 10 /l9
WBC	30.4 * 10 /l9
Neutrophils	5.8 * 10 /l9
Lymphcytes	23.1 * 10 /l9

His lymphocyte count 2 months ago was 15.3 * 10 /l and a decision to start the patient on fludarabine, cyclophosphamide, and rituximab (FCR) chemotherapy is taken.

Given the proposed treatment strategy, which of the following prophylactic medications is it most important to start?

A. Co-trimoxazole
B. Aciclovir
C. Entecavir
D. Fluconazole
E. Penicillin V

A. Co-trimoxazole

Fludarabine is a purine analogue that prevents DNA synthesis through the inhibition of ribonucleotide reductase and DNA polymerase. It is associated with profound lymphopenia, and significantly increases the risk of opportunistic infections. Patients treated with fludarabine are at particular risk of morbidity and mortality secondary to pneumocystis pneumonia. It is essential that these patients receive regular prophylactic co-trimoxazole.

Purine analogues can lead to herpes simplex, herpes zoster, and cytomegalovirus reactivation and aciclovir is often given as prophylaxis against this. Fluconazole is also frequently given as fungal prophylaxis.

Entecavir is given to patients who are hepatitis B surface antigen (HBsAg) positive. Penicillin V is given to patients with asplenia and is not routinely used in this setting.

Pneumocystis pneumonia is the most severe complication described. Co-trimoxazole is, therefore, the most essential of the medications listed above.

Question 94 of 191

A 77-year-old lady was seen in the haematology outpatient clinic for her monthly follow-up. She has been seen in the haematology clinic for the last six months having been referred by her GP following an anomaly on her blood investigations. Overall she has been feeling well though for the last three weeks she has been feeling increasingly tired. She has noted that her appetite has been reduced for the last three months though she has not lost any weight during this time. In spite of the tiredness she is still able to lead an active life, regularly enjoying long distance rambling and gardening. She denied the presence of other symptoms, including the absence of fever or night sweats. She has a past medical history comprising asthma, hypertension, type 2 diabetes mellitus and hypercholesterolaemia for which she has been prescribed felodipine 5mg M/R OD, atorvastatin 20mg ON, Clenil modulite 2 puffs BD and metformin 500mg TDS.

Examination revealed the presence of a well elderly lady who was independently mobile. Her blood pressure was 122/82 mmHg, heart rate 82bpm and temperature 36.9 Celsius. Examination of her cardiovascular and respiratory systems revealed the presence of normal heart and breath sounds and a JVP of 3cm. Examination of her gastrointestinal and lymphatic systems revealed the presence of a smooth edge 2 fingerbreadths below the left subcostal margin and bilateral small

cervical lymphadenopathy, with the maximum node size less than 1cm. Investigations reveal the following:

Results from clinic three months ago:

Hb	112 g/l
Platelets	242 * 10 /l
WBC	22.6 * 10 /l
Neutrophils	2.1 * 10 /l
Lymphocytes	19.9 * 10 /l
Eosinophils	0.4 * 10 /l
Monocytes	0.2 * 10 /l

Renal and liver function tests were normal.

Blood film: lymphocytosis with atypical lymphocytes Bone marrow aspirate: infiltration with 25% lymphocytes

Peripheral blood flow cytometry: presence of circulating clonal B-lymphocytes expressing CD5, CD19, CD20, CD 23, and an absence of FMC-7 staining

Results from clinic on this occasion:

Hb	106 g/l
Platelets	162 * 10 /l9
WBC	34.2 * 10 /l9
Neutrophils	2.3 * 10 /l9
Lymphocytes	31.5 * 10 /l9
Eosinophils	0.3 * 10 /l9
Monocytes	0.1 * 10 /l9

What is the single next best step management step?

A. Commence prednisolone therapy
B. Commence chlorambucil therapy
C. Commence fludarabine therapy
D. Commence rituximab therapy
E. Observe in clinic and repeat tests in one month

A. Commence prednisolone therapy

This lady has chronic lymphocytic leukaemia (CLL) as manifested by the high lymphocyte count, lymphocyte marrow infiltration and evidence clinically of splenomegaly and lymphadenopathy. 70% of patients are asymptomatic and patients with stage A leukaemia as with this lady [no anaemia or thrombocytopaenia and less than 3 areas of lymphoid enlargement] have a median survival of 8 years. Treatment is therefore not indicated.

Accepted indications for treatment include:

The development of anaemia +/ thrombocytopaenia

Progressive or massive splenomegaly (6cm) +/ lymphadenopathy (10cm)

Progressive lymphocytosis [50% increase in 2 months or doubling time of less than 6 months] Systemic symptoms [fever, night sweats, weight loss >10% in 6 months, extreme fatigue]

Although this lady has been complaining of tiredness, this does not in itself constitute a 'systemic symptom' given the absence of other symptoms and her strong performance status. Her lymphocyte count is rising but does not meet the criteria for treatment at present. Should treatment be indicated, this comprises chemotherapeutic agents such as chlorambucil and fludarabine, immunological agents such as rituximab and steroids in advanced disease.

Question 95 of 191

A 32-year-old patient who is 10 weeks pregnant attends for her antenatal booking clinic. This is her first pregnancy, and she tells you she has been feeling lethargic and has a poor appetite. She has no past medical history of note.

On examination, she looks pale and appears comfortable at rest. Her chest is clear, heart sounds I&II are present and her abdomen is soft non-tender. She has some oedema of both ankles bilaterally. Her blood pressure is 111/75 mmHg and her heart rate is 79/min.

Investigations in clinics are as follows:

Hb	94 g/l
MCV	69 fl
Platelets	168 * 10 /l9
WBC	9.1 * 10 /l9
Hb electrophoresis	positive HbA2
Rhesus	negative
Blood Group	AB
Na +	139 mmol/l
K +	3.9 mmol/l
Urea	7.6 mmol/l
Creatinine	99 µmol/l

What is the single most likely underlying condition?

A. Alpha thalassaemia trait
B. Beta thalassaemia trait
C. Beta thalassemia major
D. Iron deficiency anaemia
E. Sideroblastic anaemia

B. Beta thalassaemia trait

The two main differentials in this patient who has been identified as having a symptomatic microcytic anaemia during pregnancy are iron deficiency anaemia and beta thalassaemia trait. The clue that this is beta thalassaemia trait rather than iron deficiency anaemia is that the MCV is surprisingly low for the level of haemoglobin. In iron deficiency anaemia you would expect the MCV to be much higher for a fairly modest decrease in haemoglobin.

In addition, the Hb electrophoresis shows +ve HbA2 which supports the diagnosis of beta thalassaemia trait. Of course, it would be wise to send off iron studies in this patient to assess for a coexistent iron deficiency anaemia.

Question 96 of 191

A 54-year-old gentleman is reviewed 48 hours after being admitted to his local hospital with neutropaenic sepsis. He measured his temperature at home found it to be 38.2ºC. Because of this, he called the chemotherapy helpline and he was advised to attend the

emergency department who promptly admitted him under the care of the medical team.

He has a background of metastatic colorectal cancer and he has had chemotherapy ten days ago. He was started on piperacillin with tazobactam on admission. His temperature settled within 12 hours and investigations, including blood cultures, a chest X-ray, urine testing and a thorough examination did not find any source of infection. His initial neutrophil count was 0.4* 10 /l. Recent blood tests demonstrate a neutrophil count of 0.5* 10 /l. His vital parameters have all been normal since his temperature settled and he has not noticed any symptoms at any point.

What is the most appropriate management plan?

A. Convert patient to oral antibiotics and discharge
B. Keep on IV antibiotics in hospital until full course completed
C. Monitor neutrophil count in hospital and discharge when greater than 1* 109/l
D. Arrange for outpatient IV antibiotics
E. Change piperacillin with tazobactam to meropenem

A. Convert patient to oral antibiotics and discharge

The correct answer is to convert patient to oral antibiotics and discharge. This is a patient who was admitted with a fever and a low neutrophil count and therefore he was managed with empirical IV antibiotics for neutropenic sepsis. Many of these patients will not look or feel significantly unwell and in the majority of them identifying a source of the temperature can be impossible. If neutropenic they should be treated with urgent IV antibiotics and waiting for a full blood count to confirm the low neutrophil count would be inappropriate. At 48 hours the antibiotic should be reviewed and if still febrile then escalation of antibiotics should be considered If they have improved and the temperature has settled then there can be a consideration of an oral switch or if completely well can stop antibiotics altogether. NICE does not recommend keeping patients in hospital whilst waiting for their neutrophil count to improve.

Question 97 of 191

A 67-year-old gentleman presents to the emergency department following a fall. He tripped on the carpet and landed on his back. Following this he has been complaining of lower back pain, but this pain was present prior to his fall and only slightly worsened with the accident. He undergoes a CT scan which unfortunately demonstrates lytic lesions in his lumbar vertebrae. He is suspected of having multiple myeloma. He undergoes blood and urine tests which unfortunately raises further suspicion of the diagnosis. He is due to undergo a bone marrow biopsy.

What investigation prior to the biopsy can give prognostic information?

A. Serum immunofixation
B. B2 microglobulin
C. Serum corrected calcium
D. Protein electrophoresis
E. Urine electrophoresis

B. B2 microglobulin

The correct answer is B2 microglobulin. This is a patient who has unfortunately found to have multiple myeloma and is awaiting further investigation to obtain histology. B2 microglobulin elevation and fall in albumin are associated with a poor prognosis. Serum immunofixation and electrophoresis studies are useful diagnostic tools but are not as useful in terms of prognosis.

Question 98 of 191

A 45-year-old man undergoing chemotherapy mentions to the nurses that he has been feeling unwell for the last two days. He has currently having treatment for metastatic lung cancer. The nurses find that his temperature is 38.2ºC. His other observations are stable. He has been having chemotherapy via a peripherally inserted central catheter (PICC). On examination his line site appears normal, his chest his clear and his abdomen is soft and non-tender.

What is the most appropriate next step in his management plan?

A. Send a full blood count to tests neutrophil levels
B. Remove the PICC line and then observe if temperature settles
C. Remove the PICC line then discharge with IV antibiotics
D. Take blood cultures from the PICC line and peripherally then treat with IV antibiotics
E. Discharge with oral antibiotics

D. Take blood cultures from the PICC line and peripherally then treat with IV antibiotics

The correct answer is to take blood cultures from the PICC line and peripherally then treat with IV antibiotics. This is a patient on chemotherapy who has developed an asymptomatic fever at 38.2ºC. As he may be neutropenic, he should be admitted to hospital and given IV piperacillin and tazobactam, but blood cultures should be taken from any central lines that he has before doing so. If a line has more than one port then blood cultures should be taken from each port. Peripherally inserted lines should only be removed if they are shown to be the cause of infection, which is why blood cultures from these lines are important.

Question 99 of 191

A 50-year-old man is diagnosed with high-grade non-Hodgkin's lymphoma and starts his regimen of R-CHOP chemotherapy. Two days after his chemotherapy he complains of feeling increasingly weak, lethargic and generally unwell. He has developed persistent vomiting and is unable to tolerate oral fluids.

He has a history of recurrent gout but has been unable to tolerate allopurinol.

On examination, he looks unwell and pale. He seemed short of breath with a respiratory rate of 28 per minute. His temperature is 36.5ºC, heart rate 110 bpm, blood pressure 100/60 mmHg.

His heart sounds were normal. His JVP was raised by 4cm lying at 45 degrees in the bed. Examination of the chest revealed fine bibasal inspiratory crepitations. Pitting oedema was present to mid-shins bilaterally.

Abdominal examination was unremarkable.

On neurological examination, there was normal tone and sensation to all limbs. General weakness was noted.

The house officer has taken bloods:

Na+	137 mmol/L
K+	6.2 mmol/L
Urea	15 mmol/L (previously 8)
Creatinine	240 µmol/L (previously 100)
Hb	100 g/L
WBC	10.0x10^9/L
Corrected Calcium	1.95 mmol/L
Phosphate	2.3 mmol/L
Uric acid	640 mmol/L
LFTs	Normal

Chest x-ray shows congested lung fields.

ECG demonstrates tall T waves.

In view of the diagnosis which of the following is most likely to treat the hyperuricaemia? IV calcium gluconate, insulin and

A. dextrose infusion
B. Allopurinol
C. Rasburicase
D. IV fluids
E. IV electrolyte replacement

C. Rasburicase

This man has lymphoma and has presented with physical and biochemical markers suggesting established tumour lysis syndrome. He has severe electrolyte disturbance: hyperkalaemia, hypocalcaemia, hyperphosphataemia. The chest x-ray suggests pulmonary oedema and ECG indicates a degree of cardiac toxicity from the hyperkalaemia. There is also acute renal failure and hyperuricaemia.

The question asks what treatment should be used to treat the underlying condition of tumour lysis syndrome. The answer is rasburicase as he has previously been intolerant of allopurinol in the context of gout prophylaxis. All the other answers are entirely reasonable and are part of the treatment of tumour lysis syndrome but do not answer this question specifically

Question 100 of 191

An 85-year-old male is referred by the anaesthetic registrar after abnormal blood test results were noted during pre-assessment for an elective hip replacement. He is otherwise fit and well, independent with all activities of daily living and continues to drive. His past medical history includes diet controlled type 2 diabetes mellitus and hypertension. On examination, he is alert and well, reports no discomfort, pain, or non-specific malaise. No skin bruises or conjunctival pallor are noted. You note a rubbery, non-tender and firm 3cm lymph node in the left cervical chain and non-tender splenomegaly at 8cm below the costal margin. His chest is clear and normal heart sounds are noted. His blood tests are as follows, with blood tests from his GP 6 months ago in brackets:

Hb	89 (95) g/l
Platelets	78 (76) * 10 /l9
WBC	67 (32) * 10 /l9
Blood film	mature lymphocytes and smudge cells

What is the most appropriate treatment?

A. Monitor and repeat blood count in 6 months
B. Fludarabine, cyclophosphamide and rituximab treatment immediately
C. Delayed chlorambucil treatment in 6 months
D. Platelet transfusion
E. Intravenous immunoglobulin

B. Fludarabine, cyclophosphamide and rituximab treatment immediately

This patient is on the cusp of requiring immediate treatment for chronic lymphocytic leukaemia. The latest guidelines are provided by the British Committee for Standards in Haematology (BCSH) 2012 , recommending immediate treatment to commence if the patient demonstrates signs of progressive marrow failure, massive or symptomatic splenomegaly greater than 6cm below the costal margin, massive or symptomatic nodes greater than 10cm in longest diameter, progressive lymphocytosis with doubling in 6 months, autoimmune thrombocytopaenia or anaemia, or significant constitutional symptoms within the previous 6 months. It is important to note that doubling of lymphocytosis is calculated only if the initial count is greater than 30 x 109/l.

Asymptomatic patients not meeting these criteria do not benefit in long term survival when receiving immediate chlorambucil therapy versus delayed treatment . Regular blood test monitoring is more appropriate for this group of patients. Be aware that despite increased white cell counts, the mature lymphocytes are non-functional and patients are hence at increased risk of infections. Intravenous immunoglobulin may be appropriate if the patient shows features of a significant infection. Similarly, significant progressive marrow failure, demonstrated by symptomatic anaemia or thrombocytopaenia may require replacement. In this case, the patient fits criteria for immediate treatment based on his lymphocytosis doubling time and splenomegaly.

1. British Committee for Standards in Haematology (BCSH) 2012

2. Chemotherapeutic options in chronic lymphocytic leukaemia: a meta-analysis of the randomised

trials. CLL Trialists' Collaborative Group. J Natl Cancer Inst. 1999;91(10):861

Question 101 of 191

A 77-year-old female is referred to the hospitals ambulatory care clinic by her GP after 2 months of increasing generalised malaise and 'lack of energy' over the past two months. She lives with her husband and until 9 weeks ago, continued to drive and go for walks in the countryside with no limitations to her exercise tolerance. Now, she feels 'tired all the time' but denies any problems with her mood. She has no history of psychiatric disorders. Her past medical history includes hypertension (well controlled on ramipril alone), hypercholesterolaemia (well controlled on simvastatin) and chronic lymphocytic leukaemia, diagnosed 3 years ago and not requiring treatment.

On examination, she has warm peripheries with bilateral conjunctival pallor. She is alert and comfortable at rest. Non-tender lymphadenopathy in bilateral cervical chains. Her cardiovascular, respiratory, abdominal and neurological examinations are otherwise unremarkable. Her blood results are as follows:

Hb	37 g/l
MCV	87 fl
Platelets	17 * 10 /l9
WBC	44.0 * 10 /l9
Blood film	myeloblasts with elongated, needle-like cytoplasmic inclusions
Hb	72 g/l
MCV	101 fl
Platelets	70 * 10 /l9
WBC	67.0 * 10 /l9
Neut	4.0 * 10 /l9
WBC	62.0 * 10 /l9
Reticulocytes	14%
Blood film and direct agglutination test	lymphocytosis, smudge cells, reticulocytes, red cell agglutination at physiological temperature

What is the most likely cause of this patient's anaemia?

A. Cold autoimmune haemolytic anaemia 14%
B. Warm autoimmune haemolytic anaemia 75%
C. B12 deficiency anaemia 4%
D. Iron deficiency anaemia 1%
E. Microangiopathic haemolytic anaemia 6

B. Warm autoimmune haemolytic anaemia 75%

The patient presents with a borderline macrocytic/normocytic anaemia with a positive Coombs test at 37 degree temperature, suggesting an autoimmune haemolytic anaemia. The presence of red cell agglutination at a warm temperature suggests the presence of IgG on red blood cells, which in vivo leads to phagocytosis by a granulocyte: this is warm autoimmune haemolytic anaemia. Conversely, red cell agglutination at cold temperatures, typically between 0 and 4 degrees, suggests the presence of IgM and C3 component of complement, most commonly leading to direct cell lysis by the complement system: this is cold autoimmune haemolytic anaemia. A mildly raised or borderline MCV does not necessarily guarantee a macrocytic cause in this context: the high proportion of reticulocytes in the blood demonstrates increased red cell production from marrow, increasing the release of immature cells with higher corpuscular volume than mature red cells, hence the increased MCV in blood assays. Iron deficiency anaemias typically produce microcytic anaemias with target cells. Microangiopathic haemolytic anaemia (MAHA) is caused by the mechanical destruction of red cells in conditions such as thrombotic thrombocytopenic purpura, leading to fragmented red cells (schistocytes) and a typically normocytic picture with associated thrombocytopenia.

Both warm and cold autoimmune haemolytic anaemias can be idiopathic or caused by lymphoproliferative disorders. Warm agglutinins are also more commonly produced by systemic autoimmune conditions such as SLE, rheumatoid arthritis and systemic sclerosis, while cold agglutinins are also classically triggered by mycoplasma and viral infections such as infectious mononucleosis.

Question 102 of 191

A 57-year-old female presents to pre-assessment surgical clinic prior to an elective arthroscopy of her left knee that she injured while playing tennis. She is otherwise asymptomatic, has no other medical history and is a lifelong non-smoker. She drinks 10 units of alcohol per week. Recently, she has experienced hot flushes and irregular periods, which she puts down to undergoing the menopause. Examination of her cardiovascular, respiratory and abdominal systems are unremarkable.

Her blood results are as follows:

Hb	95 g/l
MCV	59 fl
Platelets	389 * 10 /l9
WBC	4.5 * 10 /l9
Red cell distribution width	13% (normal range 11.5-14.5%)
Blood film	anisocytosis, hypochromia, target cells

Which investigation is most likely to reveal the diagnosis?

A. Serum ferritin
B. Total iron binding capacity
C. Serum iron
D. Haemoglobin electrophoresis
E. Bone marrow biopsy

D. Haemoglobin electrophoresis

The patient is asymptomatic with a microcytic anaemia. Note the disproportionately lower MCV compared to the level of haemoglobin and the normal red cell distribution width: the first is a distinctive feature of thalassaemia beta minor (trait) while the second suggests that all red cells made by the marrow of similar haemoglobin quality, such as in an underlying genetic trait such as thalassaemia beta minor. In contrast, iron deficiency normally demonstrates a significant haemoglobin drop by the time MCV is at such a low value while increasing the RDW during early to mid stages of iron deficiency, as some red cells are produced normally while some are profoundly microcytic.

Diagnosis of thalassaemia beta minor is by haemoglobin electrophoresis. However, diagnosis of iron deficiency is reliant on a combination of indicators: serum iron alone is not necessarily diagnostic as it also appears in anaemia of chronic disease. Serum ferritin is perhaps the most reliable indicator of plasma and marrow iron stores but be wary that it may be increased in inflammatory states, hence mask an underlying iron deficiency anaemia. Total iron binding capacity (TIBC) is a measure of transferrin, to which iron is bound to in plasma. Again, it is a useful indicator of iron stores but can be altered by pregnancy or the oral contraceptive pill. An iron deficiency anaemia picture is generally diagnosed by a combination of all three: low serum iron, high TIBC, low ferritin.

Question 1 of 89

A 57-year-old presents with recurrent episodes of bleeding gums, nosebleeds and intermittent haematuria over the past 6 weeks. He works as an accountant, does not have any past medical history but is an active smoker of 20 pack years. He drinks occasional alcohol.

On examination, scabs and dried blood are noted on mucous membranes. No arthritis or cutaneous abnormalities are noted. The nasal bridge is unremarkable. His conjunctiva appeared pale, respiratory, abdominal and cardiovascular examination was unremarkable. His blood tests are as follows:

Na +	147 mmol/l
K +	3.2 mmol/l
Urea	7.8 mmol/l
Creatinine	70 µmol/l

What is the most likely underlying diagnosis?

A. Acute myeloid leukaemia
B. Acute lymphocytic leukaemia
C. Chronic myeloid leukaemia
D. Chronic lymphoid leukaemia
E. Myelofibrosis

A. Acute myeloid leukaemia

The diagnosis is made on blood film description of needle-like elongated cytoplasmic inclusions, known as Auer rods that are pathognomonic of acute myeloid leukaemia, with myeloblasts typical of myeloid leukaemias. Clinical features are frequently typical of cell line abnormalities secondary to marrow infiltration (shortness of breath on exertion, pallor caused by anaemia; bruising or bleeding caused by thrombocytopaenia) and infections secondary to dysfunctional white cells. Diagnosis is confirmed by bone marrow biopsy, with blast cells accounting for greater than 20% of marrow cellularity. Immunophenotyping, cytogenetic and morphological analysis guides subsequent treatment options.

Question 2 of 89

A 60-year-old female with known chronic lymphocytic leukaemia (CLL) presents with coryzal symptoms. Examination findings are unremarkable. Her blood tests are as follows:

	8 months previously	Two months previously	Today
Haemoglobin	113 g/l	108 g/l	106 g/l
White cell count	32.0 *10^9/l	50.0 *10^9/l	58.0 *10^9/l
Neutrophils	7.0 *10^9/l	4.8 *10^9/l	4.0 *10^9/l
Lymphocytes	25.0 *10^9/l	45.0 *10^9/l	54.0 *10^9/l
Platelets	358 *10^9/l	280 *10^9/l	268 *10^9/l

What is the most appropriate treatment option?

A. Chlorambucil
B. Fludarabine and chlorambucil
C. Observation
D. Prednisolone
E. Fludarabine

C. Observation

CLL is typically an indolent disease which is often managed conservatively in the first instance. Indications for treatment are multiple but include constitutional symptoms, bone marrow failure and massive lymphadenopathy. Additionally, a lymphocyte doubling time of less than 6 months is an indication for treatment, but this is not met here. Chlorambucil, fludarabine and high dose corticosteroids are all possible therapeutic options in CLL.

Question 3 of 89

A 21-year-old male is admitted to hospital after his GP identified a pancytopenia following a workup for recent fatigue and weight loss. An hour after arrival he develops a sustained nosebleed. On review, you notice oozing from his cannula sites and non-blanching purpura over his arms and legs.

What is the most likely cause of this patient's presentation?

A. Henoch-Schonlein purpura
B. Aplastic anaemia
C. Acute promyelocytic leukaemia
D. Meningococcal septicaemia
E. Idiopathic thrombocytopenic purpura

C. Acute promyelocytic leukaemia

DIC is a severe complication of acute promyelocytic leukaemia

This patient has developed disseminated intravascular coagulopathy (DIC) secondary to acute promyelocytic leukaemia (APML). This is a potentially life-threatening complication of APML that is important to be aware of in patients presenting with features of leukaemia.

Henoch-Schonlein purpura does not result in a pancytopenia or bleeding. The purpuric rash present is typically on the lower limbs and secondary to a vasculitic process. Aplastic anaemia also presents with a pancytopenia, but the features suggestive of DIC in this patient point against this as the underlying diagnosis. Meningococcal septicaemia is an important differential to consider though would not be expected to result in complete marrow suppression. Finally, idiopathic thrombocytopenic purpura causes an isolated platelet drop.

Question 4 of 89

A 25 year old man is admitted to the acute medical unit and is treated for a left lobar pneumonia. Looking through his past medical history you note he has had 3 previous admissions with similar presentations in the last 5 years. He has no other past medical history of note, apart from what he describes as 'a few' episodes of sinusitis. His blood differential, after treatment of his pneumonia, is normal. His HIV test is also negative.

What is the possible underlying diagnosis?

A. Cystic fibrosis
B. Selective IgA deficiency
C. Wiskott-Aldrich syndrome
D. Acute lymphoblastic leukemia
E. Digeorges syndrome

B. Selective IgA deficiency

Selective immunoglobulin A deficiency:

- The most common primary antibody deficiency
- Affected patients may develop recurrent chest infections, bronchitis, sinusitis or even otitis media.
- Associated with atopic disorders such as asthma and atopic dermatitis.
- Some patients may also be at risk of severe transfusion reactions.

Wiskott-Aldrich syndrome:

- Characterised by a triad of recurrent chest infections/recurrent sinus infections
- Atopic dermatitis
- Thrombocytopenia and platelet dysfunction

- Inherited as an X linked recessive condition.

Question 5 of 89

A 57-year-old man presents to his General Practitioner with persistent headaches and blurred vision. The symptoms have been present over the past six months but have worsened in recent weeks. On close questioning, the patient also reported a feeling of general fatigue and intermittent muscle aches.

One year previously, the patient had been diagnosed with obstructive sleep apnoea secondary to morbid obesity and had been provided with non-invasive ventilation to use at night. However, the patient admitted that he rarely used this equipment due to a dislike for the tight face mask. Despite dietary and lifestyle advice the patient had gained 6 kg over the past year and had a BMI of 41 kg / m².

Neurological examination including fundoscopy was unremarkable. There were no tender or inflamed joints. Blood tests requested by the GP are detailed below.

Haemoglobin	195 g/L
White cell count	7.5 * 10 /l9
Neutrophils	5.7 * 10 /l9
Lymphocytes	0.9 * 10 /l9
Platelets	195 * 10 /l9
Packed cell volume	0.60
Urea	5.9 mmol / L
Creatinine	110 µmol / L
Sodium	135 mmol / L
Potassium	4.1 mmol / L
eGFR	68 ml / min

Review of a full blood count performed 4 months previously was remarkable for previously unnoticed elevated PCV of 0.56. The patient was urgently referred to haematology for further management.

What is the most appropriate treatment for this patient's erythrocytosis?

A. Aspirin
B. Venesection
C. Hydroxyurea
D. Improved compliance with nocturnal non-invasive ventilation
E. Referral to weight management service

B. Venesection

This patient has a secondary erythrocytosis secondary to hypoxia associated with his obstructive sleep apnoea. He is presenting with significant symptoms of hyperviscosity and should be considered to be at significant risk of thrombotic complications.

Evidence from small case series suggests that erythrocytosis secondary to OSA should be treated with venesection in the presence of hyperviscosity symptoms or a PCV > 0.56. A target PCV of 0.50-0.52 has been shown to increase exercise tolerance.

Aspirin is the mainstay of treatment in polycythaemia vera and cytoreductive treatments such as hydroxyurea are used in high-risk cases.

While weight-loss and improved compliance with OSA treatment may improve erythrocytosis these interventions are likely to require significant time prior to yielding any symptomatic benefit.

Question 6 of 89

You are working in haematology. A 72-year-old man has been referred to you by the general surgeons. He recently had a CT scan for weight loss and a two month change in bowel habit. This showed no lesions within the bowel but did demonstrate some mesenteric lymphadenopathy. The largest lymph node was 4 cm in diameter. He is otherwise well and has a background of hypertension and diet controlled diabetes. He subsequently underwent a CT guided biopsy (histology report below).

The lymph node biopsied lacks a mantle zone and is made up of a predominant population of centrocytes with few tangible body macrophages. Immunohistochemistry confirms strong positivity for CD20 as well as CD70a, CD10, BCL2 and BCL6. The proliferation index (Ki-67) is low, no more than 20%.

What is the most likely diagnosis?

A. Nodular sclerosing lymphoma
B. Lymphoplasmacytic lymphoma
C. Follicular lymphoma
D. Adenocarcinoma of the large bowel
E. Diffuse large B cell lymphoma

C. Follicular lymphoma

The correct answer here can be worked out based on the Ki-67 index. This is the proliferation index and is a marker (antigen) of the cancer cells metabolic rate. In high grade lymphomas such as diffuse large B cell lymphoma the Ki-67 will be high (>45%) therefore answer 5 is wrong. In low grade lymphomas such as follicular lymphoma the Ki-67 is low (<40%).

Follicular lymphoma (a form of non Hodgkin's lymphoma) often presents as incidentally found enlarged lymph nodes and may present without the B symptoms often seen in Hodgkin's lymphoma. It can undergo a transformation at any stage into a high grade lymphoma.

Answer 1 is wrong because as it is a form of Hodgkin's lymphoma the histology report would have mentioned the presence of reed-sternberg cells. Answer 2 is Waldenstrom's macroglobulinemia and presents with an IgM gammopathy. Answer 4 is wrong because an adenocarcinoma of the large bowel would have most likely been seen on a CT scan.

Question 7 of 89

A 72-year-old woman presents to the emergency department following a fall. On examination, her right leg is shortened and externally rotated and she is unable to weight bear. A hip X-ray demonstrates a fractured neck of femur which appears pathological. She has no history of cancer. Following a dynamic hip screw insertion, she recovers well. She has blood tests sent for FBC, U&E, LDH, calcium, albumin, uric acid, serum electrophoresis, immunoglobulins and ESR. She has had a chest X-ray which was normal.

What additional tests should be requested to complete the initial investigations of the pathological nature of the fracture?

A. MRI whole spine
B. MRI hip
C. Urinary electrophoresis

D. Trephine biopsy
E. Bone marrow biopsy

C. Urinary electrophoresis

The correct answer answer is urinary eletrophoresis. This is a patient with a pathological fracture and at high risk of myeloma and needs to be fully investigated.

The following tests are needed to complete a myeloma screen:

FBC, ESR, U&E, calcium, albumin, uric acid

Serum protein electrophoresis Urine protein electrophoresis Immunoglobulin levels

Plain X-ray of symptomatic areas

If initial investigations are suggestive of myeloma then bone marrow aspirate and trephine biopsies are indicated, as well as immunofixation of the serum and urine to demonstrate the nature of the paraprotein.

MRI would be contra-indicated due to the recent operation

Question 8 of 89

A 30-year-old gentleman presents with acute lethargy and shortness of breath. He reports cutting his leg on a wooden splinter in a bench with a red area that arose in the leg and spread rapidly. Two days later his leg remained painful and he started to develop chills and was brought into the hospital by concerned family.

On examination, he is pale and clammy with a capillary refill time of 4 seconds. His chest is clear but his breathing is shallow and rapid. His heart rate is 123 beats/min and is regular while his blood pressure is 85/65 mmHg. His leg shows the cut which is now raised and red-purple with a collection of pus under the skin. His cannula site is oozing blood. He receives three litres of intravenous fluid and is started on vancomycin and gentamicin intravenously.

Hb	130 g/l
Platelets	110 * 10 /l9
WBC	34.0 * 10 /l9
CRP	459 ng/ml
PT	18 seconds
APTT	45 seconds
Fibrinogen	0.1
Chest x-ray	patchy bilateral infiltrates
Wound swab	Streptococcus pyogenes

What is the explanation of the coagulation?

A. Disseminated intravascular coagulopathy (DIC)
B. Activation of thrombin by insect venom
C. Haemodilution by intravenous fluids
D. Haemophilia A
E. Von Willebrand disease

A. Disseminated intravascular coagulopathy (DIC)

Deranged coagulation in sepsis -> DIC

This patient is acutely septic and has deranged coagulation. Haemodilution would not deplete fibrinogen severely. Haemophilia A and Von Willebrand disease have a mildly raised APTT only but normal fibrinogen level. There is no history of an insect bite making it unlikely.

DIC is a consequence of severe sepsis where the clotting cascade is activated throughout the body forming small thrombus throughout the body but depleting the clotting factors. Specifically, there is a low fibrinogen. There are rare cases of snake venom activating the clotting cascade in a manner similar to DIC but there is no recall of a snake and is rare in the UK.

Question 9 of 89

A patient has been admitted with left lower limb deep vein thrombosis. He was diagnosed by the FY1 who has efficiently started him on warfarin.

Two days after initiation you are asked to see this gentleman who has developed skin necrosis over his right thigh.

What is the most likely cause of his skin necrosis?

A. Antiphospholipid syndrome
B. Heparin induced thrombocytopenia (HIT) type II
C. Excessive serum Antithrombin III
D. Acquired haemophilia
E. Protein C deficiency

A. Protein C deficiency

Warfarin induced skin necrosis is rare but very severe. Be reminded that warfarin inhibits production of the vitamin K dependent coagulation factors including factors II, VII, IX and X but also the natural anticoagulants, proteins C and S. The first factors affected by warfarin are the anticoagulants, making warfarin temporarily pro-thrombotic during induction, in its initial few days of use and that is why it is advised to start heparin concurrently with Warfarin. Various theories have been postulated as to the cause of this problem one of which is a background of congenital or acquired protein C, S or Antithrombin III deficiency.

Question 10 of 89

A 38-year-old female presents to the emergency department with pain in her right leg, which she attributes to tripping up and landing on the floor when she went hiking with her boyfriend approximately 1 week ago. She does not recall any insect bites but has become increasingly concerned as her leg has become more swollen and tender in the calf region.

She has no significant medical history but has been recovering from an episode of pneumonia for which her GP prescribed her clarithromycin. Her only other medication is the oral contraceptive pill which she started about 1 month ago. She consumes alcohol socially at the weekends and smokes approximately 10-15 cigarettes a day. On physical exam she is afebrile and her other vital signs are within normal limits. She is able to ambulate in the emergency department without significant issues, and there are no obvious skin breakages or significant bony deformities. You note that her left leg is significantly swollen compared to the right leg and there is evidence of pitting oedema and erythema. Passive dorsiflexion of her left foot leads to significant pain.

What is the next best step in the management of this patient?

A. Obtain a doppler ultrasound scan of her left lower limb
B. D-dimer test
C. Start her empirically on oral amoxicillin for probable lower limb cellulitis
D. X-ray her left tibial and fibula
E. Reassure her and advise her to take regular paracetamol

A. Obtain a doppler ultrasound scan of her left lower limb

If a 2-level DVT Wells score is ≥ 2 points then arrange a proximal leg vein ultrasound scan within 4 hours

This patient most likely has a left lower limb deep vein thrombosis. Her important risk factors include the fact that she is taking the oral contraceptive pill and is a smoker, which combined leads to a significantly increased risk for venous thromboembolic complications. In fact, smoking is a contraindication to starting the oral contraceptive pill in females greater than the age of 35 years. In addition, physical exam findings are also concerning for a deep vein thrombosis. Although we could start investigating her by doing a D-dimer test, if this is normal she still has a high pretest probability of deep vein thrombosis and we could therefore not confidently exclude this diagnosis. Consequently, the best way to confirm or refute a diagnosis of deep vein thrombosis, in this case, would be obtaining a Doppler ultrasound scan of her leg. A D-dimer would not necessarily be wrong, but even if this returned as normal she is at considerable risk of deep vein thrombosis and should have a doppler ultrasound scan done anyway. In addition, she is being treated for pneumonia which is likely to confound the results of the D-dimer test anyway.

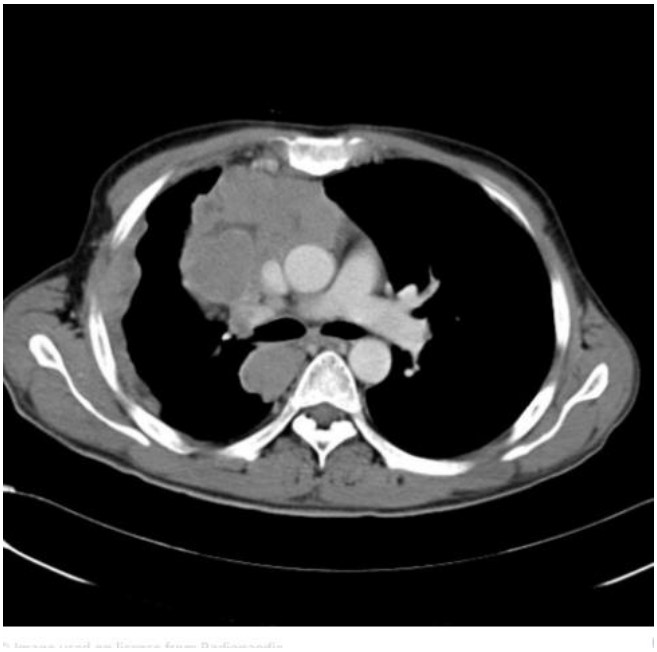
Although she does have swelling and erythema of her lower limb, she is afebrile and her clinical picture does not fit that of cellulitis.

She is ambulant and is unlikely to have sustained any significant bony injuries to her tibia and fibula, particularly as the mechanism of her injury was not very severe. Fractures of the tibia/fibula typically require a more significant mechanism of injury such as motor vehicle accidents.

It would be inappropriate to reassure her and advised her to take regular analgesia, as she is at significant risk of deep vein thrombosis and this needs to be excluded first.

Question 11 of 89

A 51-year-old man is investigated for a chronic cough, chest pain and dyspnoea. He also reports some difficult swallowing bread and meat for the past two weeks. He has no past medical history of note although has smoked for the past 30 years. A CT scan is requested:



What is the most likely diagnosis? Sarcoidosis

A. Lung cancer
B. Cardiac myxoma
C. Oesophageal cancer
D. Thymoma

A. Thymoma

The CT slice at the bifurcation of the main bronchus shows an invasive thymoma presenting as an anterior mediastinal mass.

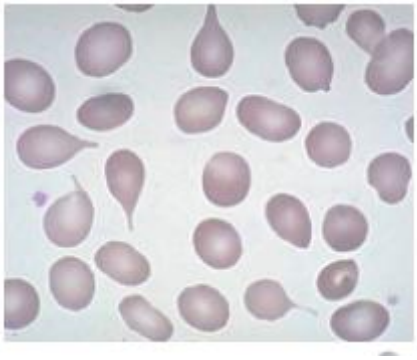
The differential diagnosis of an anterior mediastinal mass includes:

- thymoma
- lymphoma
- thyroid and parathyroid malignancies
- germ cell tumours e.g. teratomas
- thoracic aortic aneurysm

Question 12 of 89

A 77-year-old man is referred to haematology for investigation of anaemia. For several months he has been complaining of fatigue and weight loss. His GP has already arranged upper and lower gastrointestinal (GI) endoscopy which has been reported as normal.

His blood film is shown below:



What is the most likely diagnosis?

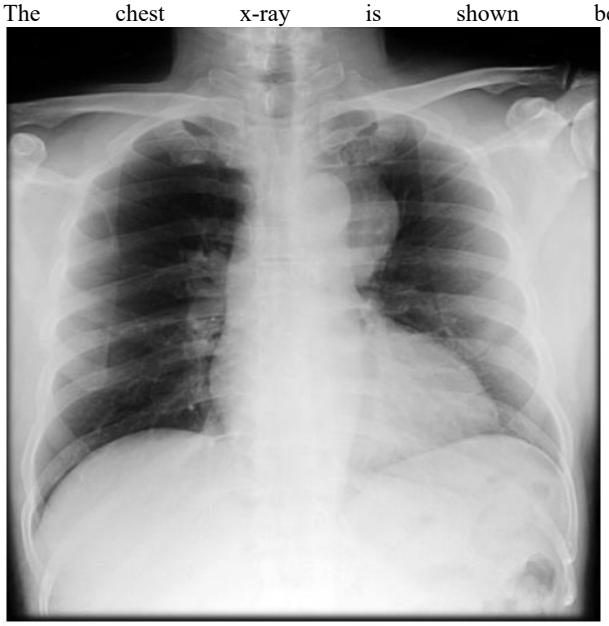
A. Chronic lymphocytic leukaemia
B. Myelofibrosis
C. Iron deficiency anaemia (bleeding from non-GI source)
D. Hyposplenism
E. Autoimmune hemolytic anaemia

B. Myelofibrosis

The blood film shows the typical 'tear-drop' poikilocytes of myelofibrosis.

Question 13 of 89

A 47-year-old man is referred to the respiratory clinic with a 3 month history of cough associated with retrosternal chest pain. A chest x-ray requested by his GP has been reported as abnormal. The chest x-ray is shown below



What is the most likely diagnosis?

A. Oesophageal cancer
B. Cardiac myxoma
C. Thymoma
D. Lung cancer
E. Sarcoidosis

C. Thymoma

The chest x-ray demonstrates a soft tissue density projecting to the left of the mediastinum. The distal part of the arch and proximal descending aorta can be seen as separate suggesting it is located anterior to these structures.

A MRI scan from the same patient is shown below:

MRI confirms the presence of an anterior mediastinal mass without convincing macroscopic invasion

Question 14 of 89

A 62-year-old woman presents to the haematology clinic. She has had lower back pain, which has been progressive in nature. She has also been noted to develop unexplained anaemia. Her initial protein electrophoresis and serum-free light chain assays raised suspicion of multiple myeloma. She has a past medical history of transient ischaemic attacks and hypertension. She takes clopidogrel, amlodipine and ramipril.

What imaging should be offered to further assess her?

A. Lumbosacral X-rays
B. Skeletal survey
C. Bone marrow ultrasound
D. Whole body MRI
E. PET scan

D. Whole body MRI

The correct answer is whole body MRI. NICE advises that all patients suspected to have a diagnosis of myeloma should be offered whole body MRI as first-line imaging, and only consider whole body CT if the patient declines MRI or is unable to have it. Skeletal survey should only be considered if CT and MRI are both not possible. Fluorodeoxyglucose positron emission tomography CT (FDG PET CT) can be considered once a diagnosis is confirmed

Question 15 of 89

A 69-year-old gentleman presented for routine follow-up in the oncology clinic. He has metastatic poorly differentiated adenocarcinoma of unknown primary. He commenced palliative chemotherapy with oxaliplatin and fluorouracil two months ago. The most recent CT scan demonstrated stable disease.

Ten days ago he was admitted to the local emergency department with fever and diagnosed with neutropenic sepsis, of which the cause was not clear. He was admitted for IV Tazocin for five days then discharged with co-amoxiclav and filgrastim (G-CSF). He currently feels well. On examination, there are no abnormalities.

Observations:

Saturations	95%
Respiratory rate	14/min
Blood pressure	152/83mmHg
Heart rate	69/min
Temperature	37.3°C

Blood tests:

14 days ago	Today	
Hb	135g/l	124g/l
Platelets	322* 10 /l 9	285* 10 /l9
WBC	0.2* 10 /l 9	23.6* 10 /l9

What is the most appropriate course of action?

A. Restart oral co-amoxiclav
B. Arrange admission for IV tazocin
C. Arrange admission for IV meropenem
D. Start prednisolone
E. Stop filgrastim (G-CSF)

A. Stop filgrastim (G-CSF)

The correct answer is to stop filgrastim. Filgrastim stimulates a white cell count which can increase far above the normal range, and the white cell count will return to normal once it is stopped. The key here is that the patient is clinically well, and further antibiotics are unnecessary

Question 16 of 89

A 67-year-old female presents with 4-month history of increasing lethargy and malaise. She has no past medical history and travels widely, last visiting the Middle East one week prior to this admission, returning with a respiratory tract infection that appears to be resolving. She is a lifelong non-smoker and does not drink alcohol to excess. Over the past two weeks, she reports increasing bilateral persistent headache associated with binocular visual blurring. In addition, she describes a non-specific abdominal discomfort without any changes in bowel habit.

On examination, you note bilateral axillary lymphadenopathy and conjunctival pallor. Cardiovascular and respiratory system examinations were unremarkable. Neurological examination is unremarkable. Fundoscopy reveals dilated tortuous retinal veins. Abdominal examination reveals hepatosplenomegaly. Lastly, you note areas of purpura around her left anterior shin and her right upper arm. A chest radiograph is unremarkable.

Her blood results are as follows:

Hb	87 g/l
MCV	79 fl
Platelets	190 * 10 /l9
WBC	3.4 * 10 /l9
Na +	142 mmol/l
K +	4.5 mmol/l
Urea	7.6 mmol/l
Creatinine	89 µmol/l
Adj Calcium	2.47 mmol/l
Phosphate	1.34 mmol/l
LDH	1890 (normal range 140-280 units/L)
Serum electrophoresis	IgM paraprotein band at 5.4 g/L

A bone marrow biopsy demonstrates 14% infiltration of lymphoplasmacytic cells

What is the most likely diagnosis?

A. Waldenstrom's macroglobulinaemia
B. Multiple myeloma
C. Monoclonal gammopathy of unknown significance (MGUS)
D. Chronic lymphocytic leukaemia (CLL)
E. Upper respiratory tract infection (URTI)

A. Waldenstrom's macroglobulinaemia

There is an enormous IgM paraprotein band on serum electrophoresis, immediately suggesting the differentials to narrow to Waldenstrom's macroglobulinaemia, multiple myeloma and MGUS. The patient is symptomatic, has bone marrow involvement of greater than 10% with IgM band greater than 3g/L, ruling out MGUS. The key to this diagnosis is differentiating between myeloma and Waldenstrom's: it is particularly rare (but not impossible) for an IgM-secreting plasma cell clone in myeloma but this accounts for only 0.5% of all multiple myelomas. Secondly, clinically, the patient demonstrates signs of hyperviscosity syndrome and splenomegaly, both of which are much more common in Waldenstrom's than myeloma. Thirdly, there is a lack of bone symptoms and renal involvement with normal serum calcium: bone lesions are significantly more common in multiple myeloma. Fourthly, fundoscopic tortuous and dilated veins are classical in hyperviscous patient with Waldenstrom's macroglobulinaemia. The diagnosis is clinched on bone marrow biopsy, demonstrating lymphoplasmacytic cells instead of plasma cells, confirmed by cell immunophenotyping.

CLL should not result in a paraprotein band, URTI may result in a rise in IgA but should not result in bone marrow involvement.

Question 17 of 89

A 34-year-old male presents with a 4 day history of bloody diarrhoea and vomiting, fevers and associated with occasional abdominal cramps. He reports no other symptoms. He reports no previous history of gastrointestinal disease; there is no family history of inflammatory bowel disease. He has no past medical history except for a left knee arthroscopy following an injury playing football 7 months ago. He is a lifelong non-smoker, drinks 14 units of alcohol a month, has not travelled abroad in the past year and last ate outside of his home a week ago during a barbecue at his brother's house.

On examination, he appears dehydrated. There is mild generalised abdominal tenderness with increased bowel sounds. Respiratory and cardiovascular examinations were unremarkable. His blood tests are as follows:

Hb	92 g/l
MCV	90fl
Platelets	49 * 10 /l9
WBC	14.2 * 10 /l9
Neutrophils	12.8 * 10 /l9
Blood film	schistocytes, reticulocytosis

Direct antiglobulin test	Negative
Urea	14.9 mmol/l
Creatinine	159 µmol/l
CRP	82 mg/l

What is the cause of this patient's blood abnormalities?

A. Microangiopathic haemolytic anaemia
B. Cold autoimmune haemolytic anaemia
C. Warm autoimmune haemolytic anaemia
D. Iron deficiency anaemia
E. Acute myeloid leukaemia

A. Microangiopathic haemolytic anaemia

The first recognition in this patient is the underlying syndrome: blood film with fragment red cells (schistocytes), thrombocytopaenia acute kidney injury, pyrexia and bloody diarrhoea, should strongly suggest haemolytic uraemia syndrome-thrombotic thrombocytopaenia purpura spectrum (HUS-TTP) in the absence of alternative unifying causes. In this case, gastrointestinal infection by Campylobacter from the recent barbecue, producing Shiga toxins and resulting in endothelial damage, is a strong possible culprit. The patient has a normocytic anaemia with red cell fragmentation and increased reticulocyte production, suggestive of rapid mechanical destruction and the bone marrow releasing immature red cells in (unsuccessful) compensation. This represents microangiopathic haemolytic anaemia (MAHA) in the context of HUS-TTP.

Both cold and warm autoimmune haemolytic anaemias should produce a positive direct antiglobulin test (Coombs): addition of a Coombs reagent containing antihuman globulin should agglutinate red cells IgM and IgG antibodies bound to in cold and warm autoimmune haemolytic anaemias respectively. Iron deficiency anaemia typically produces microcytic anaemias with target cells; there are no blast cells suggestive of leukaemia.

Question 18 of 89

A 23-year-old medical student went to Uganda on his elective but has had to return to the UK early due to illness. He had been careful to take malaria prophylaxis and slept under a mosquito net. He was using primaquine due to previous intolerable side effects with doxycycline. He was complaining of central abdominal pain and had noticed jaundiced sclera in the few days prior to returning to the UK. There is no relevant past medical history and he takes no regular medication. He is a non-smoker and drinks 2-4 units of alcohol weekly.

Observations show a blood pressure of 110/73 mmHg and heart rate of 98 beats per minute. He is apyrexial, has a respiratory rate of 16 per minute and oxygen saturations of 94% on room air.

On examination, he is pale and jaundiced with yellow sclera. There is no cyanosis. His chest sounds clear and heart sounds are normal with nil added. The abdomen is soft, generally tender but with no guarding or peritonism. Bowel sounds are normal.

Bloods show the following:

Haemoglobin	86 g/L	Sodium	139 mmol/L
Platelets	188 x10^9/L	Potassium	3.6 mmol/L
White cell count	11.0 x10^9/L	Urea	3.0 mmol/L
Neutrophils	8.5 x10^9/L	Creatinine	62 micromol/L
Reticulocytes	11%	Albumin	34 g/L
CRP	7 mg/L	Bilirubin	67 micromol/L
ALT	21 iu/L		
Alkaline Phosphatase	40 iu/L		

Peripheral blood film:

Heinz bodies seen with methyl violet staining.

Bite and blister cells also present.

What is the most likely diagnosis?

A. G6PD deficiency
B. Plasmodium falciparum infection
C. Mycoplasma pneumoniae
D. Hereditary spherocytosis
E. Lead poisoning

A. G6PD deficiency

This student has acute haemolytic anaemia (anaemia, reticulocytosis and raised bilirubin with normal ALT). Answers A, C, D and E are all causes of haemolytic anaemia.

The blood film is the main diagnostic tool to differentiate between these answers. Heinz bodies, bite and blister cells are all seen in acute haemolysis associated with G6PD deficiency. The acute haemolysis has been triggered by antimalarial treatment (usually primaquine).

A blood film of hereditary spherocytosis shows spherocytes and reticulocytes. In lead poisoning, there should be dimorphic cells with ring granules on Perl's staining.

Plasmodium falciparum is a common form of malaria that multiplies in the liver. Infection with this can cause anaemia with abnormal liver function tests (LFTs). Persons with G6PD deficiency are somewhat protected from infection with *Plasmodium falciparum* and *Plasmodium vivax* malaria.

G6PD deficiency is X-linked and is more prevalent in Mediterranean populations.

Question 19 of 89

A 51-year-old man presents with dysuria and a low grade fever. He is prescribed a course of Nitrofurantoin for a suspected urinary tract infection. He has a history of ischaemic heart disease for which he takes aspirin and atorvastatin. The following day, he notices that his urine has become very dark and he feels breathless and more unwell.

Bloods show:

Hb	78 g/L
WCC	14.1 x 10^9/L
Neutrophils	13 x 10^9/L
Platelets	280 x 10^9/L
Bilirubin	87 mg/dL
ALT	45 IU/L
Alkaline phosphatase	73 IU/L
Urea	5 mmol/L
Creatinine	80 µmol/L

Blood film microscopy comments on the presence of Heinz bodies.

What is the underlying diagnosis?

A. Hereditary spherocytosis
B. Paroxysmal nocturnal haemoglobinuria
C. Haemolytic uraemic syndrome
D. Urinary sepsis secondary to E. coli
E. Glucose-6-phosphate dehydrogenase deficiency (G6PD)

A. Glucose-6-phosphate dehydrogenase deficiency (G6PD)

The blood tests reveal anaemia with a bilirubin rise, which indicates haemotlyic anaemia. Heinz bodies are red cell inclusions consisting of denatured Hb; they are a feature of oxidative stress. Nitrofurantoin is one of many drugs that can cause haemolytic crisis in G6PD deficiency. Heinz bodies would not usually be seen on the blood films of the other conditions.

Question 20 of 89

A 26 year old female who is 14 days post-partum (spontaneous vaginal delivery) presents to your medical admissions unit with her partner who is worried that she is confused. She is unable to provide any history but her partner tells you that she has gradually gotten worse over the past few days. Her observations are as follows: temperature 38ºC, pulse 90/min, blood pressure 154/88 mmHg, respiratory rate 16/min, sats 99% on room air.

On examination, she looks pale. Her chest is clear and abdomen is soft, non-tender. She has multiple bruises on her arms. Her blood results are pending.

What is the most likely diagnosis?

A. Haemolytic uraemic syndrome
B. Thrombotic thrombocytopenic purpura
C. Idiopathic thrombocytopenic purpura
D. Retained products of placenta
E. Disseminated intravascular coagulation (DIC)

B. Thrombotic thrombocytopenic purpura

Thrombotic thrombocytopenic purpura is associated with fever, anaemia, thrombocytopenia, renal failure and confusion. Pregnancy and the post-partum state account for about 20% of cases seen.

Haemolytic uraemic syndrome is not associated with fever and confusion. Retained products of placental is more unlikely as her abdomen is soft, non-tender. DIC would be a differential diagnosis but is not the most likely diagnosis here. Idiopathic thrombocytopenic purpura would not cause confusion.

Question 21 of 89

A 52-year-old female with acute lymphoblastic leukaemia in on her third cycle of chemotherapy. She is admitted to the ward after developing a temperature of 38.7ºC before her fourth cycle. She feels well in herself but has ongoing trouble with diarrhoea and mucositis. At present, her stools are type four on the Bristol stool chart and her mouth ulcers are being treated with a lidocaine/nystatin topical solution. She denies any cough, sore throat or urinary symptoms.

On examination, her abdomen is soft and non-tender with normal bowel sounds. Her chest is clear with air entry heard throughout. She has no murmurs, joint effusions or areas of cellulitis. Her mouth contains multiple ulcers with areas of straw colored exudate overlying them.

Hb	110 g/l
Platelets	60 * 10 /l9
WBC	1.1 * 10 /l9
Neuts	0.5 * 10 /l9

Blood culture (1st)	Staphylococcus epidermidis
Blood culture (2nd)	no growth
Chest X-ray	clear lung fields, normal cardiac contour
Nasopharyngeal PCR	negative
Urine dip	negative for leucocytes and nitrites

Which investigation is most likely to elicit the cause of the fever?

A. Sputum culture
B. Urine culture
C. Blood culture
D. Stool sample
E. Swab mouth ulcer

A. Swab mouth ulcer

Mucositis can be a source of neutropenic sepsis

This patient has neutropenic sepsis of unknown source. In neutropenic patients, almost any site

can be the source. From the history there is diarrhoea but her stools are currently normal. There

are no urinary symptoms and the dipstick is normal making the urine unlikely to culture an

organism. Ideally, three blood cultures should be completed in pyrexia of unknown origin so this is

a useful suggestion. Sputum culture is impossible if there is no productive cough and would need

to be induced by bronchoscopy.

Importantly, we are told there are mouth ulcers and this represents a break in the protective lining

through which oral commensal bacteria can enter the blood stream and trigger sepsis. Therefore,

a swab should be taken for bacterial culture and for viral PCR from the ulcer site.

Question 22 of 89

A 45-year-old lady presents to the Emergency Department progressive shortness of breath for the last three days. It is worse on activity but is not associated with any cough or wheeze. She has a past medical history of asthma and HIV, for which takes antiretroviral medication regularly. At her last clinic appointment two weeks ago, she was found to have oral candida and so was given a 2 week course of nystatin and started on dapsone for prophylaxis of pneumocystis jirovecci pneumonia. She is a non-smoker.

On examination, her lips and nail beds have a bluish tinge and she is visibly breathless. Her respiratory rate is 26 per minute and on pulse oximetry her saturations are 91% on air both at rest and on exercise. Her temperature is 36.5ºC and she has not felt feverish. On auscultation she has vesicular breath sounds with minimal wheeze and normal heart sounds with no murmurs. She has no ankle oedema and JVP is not raised. There is no evidence of oral candidiasis and no lymphadenopathy. Her calves are soft and non-tender.

A chest x-ray shows clear lung fields with no focal consolidation or lymphadenopathy. ECG is sinus rhythm at 90 beats per minute with normal complexes throughout.

Arterial blood gas on air:

pH	7.51
PaO2	13.7 kPa
PaCO2	3.34 kPa
HCO3-	22.1 mmol/l
BE	-3.3 mmol/l
sO2	97%
Hb	113 g/l
Na+	143 mmol/l
K+	3.7 mmol/l
Glu	5.2 mmol/l
Lac	1.9 mmol/l

What is the most likely diagnosis?

A. Acute asthma
B. Carbon monoxide poisoning
C. Methemoglobinemia
D. Pneumocystis jirovecii pneumonia
E. Pulmonary embolus

C. Methemoglobinemia

This lady has shortness of breath with low saturations on pulse oximetry but normal PaO2 and saturations on arterial blood gas. This combined with a bluish discolouration and normal chest examination point towards a diagnosis of methemoglobinaemia, a known side effect of the dapsone on which she has been started.

In exacerbation of asthma, one would expect wheeze and a low PaO2. Carbon monoxide poisoning typically results in cherry red appearance. This lady does not have any history of suggest pulmonary embolus and one would again expect a low PaO2, associated with a tachycardia. Pneumocystis pneumonia would be unlikely on prophylaxis, and there may be x-ray changes and drop in saturations on exercise.

Question 23 of 89

A 44 year old female patient is admitted to the oncology ward to undergo chemotherapy for Diffuse Large B-Cell lymphoma stage IVb. She had originlly presented to her GP with intermittent abdominal bloating and constipation and occasional shortness of breath. She also reported having to often get up in the middle of the night to change the bed clothes due to drenching sweats. Her GP had been concerned by these symptoms and had organised an immediate chest X-ray to be undertaken at the nearby hospital.

Chest X-ray

large mediastinal mass with clear lung fields.

On receiving this report the GP arranged an urgent appointment with a local haematologist as he suspected that the patient was suffering from lymphoma. She was seen only 4 days later. Given the clinical history the team at the hospital arranged some urgent investigations.

Hb	9.5 g/dl
Platelets	140 * 10 /l9
WBC	36.5 * 10 /l9
Lactate Dehydrogenase	2540IU/l

CT-guided Lymph node biopsy

cells are large, with prominent nucleoli and abundant cytoplasm and many mitoses expressing

CD19 and CD20 markers

PET scan

large extra-nodal disease bulks most notable in the ileo-caecal area and in the mediastinum. Overall bulky disease in keeping with the diagnosis of advanced stage lymphoma.

The patient is admitted to receive cycle one of R-CHOP chemotherapy under close monitoring.

What electrolyte abnormalities would suggest tumour lysis syndrome?

A. High Potassium, high Calcium, low Phosphate
B. Low Potassium, high Calcium, low Phosphate
C. High Potassium, low Calcium, high Phosphate
D. Low Potassium, low Calcium, high Phosphate
E. Low Potassium, low Calcium, low Phosphate

C. High Potassium, low Calcium, high Phosphate

Question 24 of 89

A previously healthy 68-year-old male patient is referred by his GP to the general medical clinic. He has mixed symptoms of pain in multiple areas, including his upper arm, neck and legs. This has worsened over a period of months and seems not to have been helped with multiple analgesics, including paracetamol, codeine phosphate and ibuprofen. In this time the patient has also become increasingly short of breath.

A full work up is undertaken and the results are shown -

Hb	9.4 g/dl
Platelets	174 * 10 /l9
WBC	8.4 * 10 /l9
Na +	136 mmol/l
K +	4.7 mmol/l
Urea	8.4 mmol/l
Creatinine	125 µmol/l
Corrected calcium	2.9mmol/l
Albumin	34g/L

Kappa light chains detected Lambda light chains absent

IgG elevated IgA normal IgM normal

Urine Bence Jones proteins detected

Skeletal survey multiple osteolytic lesions seen throughtout axial skeleton including on the right humerus, thoracic spine and both femurs.

Given the presumed diagnosis, what tests are most relevant for staging of the condition?

A. Calcium, x-rays and creatinine
B. Free light chain level
C. Renal function
D. B2-microglobulin and albumin
E. Haemaglobin and albumin

D. B2-microglobulin and albumin

The diagnosis here is multiple myeloma. Myeloma is a plasma cell dyscrasia that is more common in men than women. It is most common in elderly populations. The affects of myeloma can easily be remembered by the tetrad of high calcium (c), renal disease (r), anaemia (a) and bone pain (b) (crab). The original staging system was known as the Durie-Salmon Staging system which was developed in 1975. It is still commonly used as a supplementary measure but it's role in staging has been replaced by the International Staging System (ISS) that was implemented by the International Myeloma Working Group in 2005.

Question 25 of 89

A 70 year-old woman presents with severe back pain which has been worsening over the last month. Prior to this she has never suffered from back pain. She has been lethargic, and her husband notes some intermittent confusion. A systemic enquiry reveals long standing exertional breathlessness, and constipation. She has no other bowel or bladder disturbance.

Her background includes chronic obstructive pulmonary disease, which is managed by her GP. She gave up smoking two years ago. Her well woman check up 12 months ago was entirely normal, aside from a slightly raised cholesterol which is being management with diet.

On examination, she has a normal gait. There is some mild tenderness over L3/L4 vertebra with no lower limb neurological deficit. Cardiorespiratory examination reveals an ejection systolic murmur, with a normal second heart sound.

Hb	90 g/l	Na +	135 mmol/l	Bilirubin	5 µmol/l
Platelets	200* 10 /l 9	K +	5.5 mmol/l	ALP	101 u/l
WBC	10 * 10 /l 9	Urea	15 mmol/l	ALT	40 u/l
Neuts	8 * 10 /l 9	Creatinine	230 µmol/l	corrected calcium	2.7 u/l
ESR	40 mm/hr				

What is the most likely diagnosis?

A. Multiple myeloma
B. Monoclonal gammopathy of undetermined significance
C. Non-Hodgkin's, lymphoma
D. Paget's disease
E. Renal cell carcinoma with spinal metastases

A. Multiple myeloma

Multiple myeloma is malignant proliferation of plasma cells, producing a monoclonal protein detected in blood and/or urine; this causes organ or tissue damage. The median age of presentation is 70 years old.

Presenting clinical features include symptoms of:

Impaired renal function- from light chain deposition from plasma cells, other causes include amyloid deposition, dehydration, hypercalcaemia, hyperviscosity, and nephrotoxic drugs Anaemia

Hypercalcaemia- myeloma cells cause an increased production of osteoclast activating factors and cytokines that inhibit osteoblast differentiation

Recurrent infections- decreased humoral immunity

Hyperviscosity symptoms (headaches, epistaxis, blurred vision, and confusion)- high paraprotein levels

Bone pain

Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic condition thought to precede multiple myeloma.

Question 26 of 89

Matthew is an 18-year-old man presenting with diarrhoea. The diarrhoea has been ongoing for the past 7 days and his stool is described as a type 6-7 stool on the Bristol stool charts. He did not note any blood or mucous accompanying his diarrhoea. There is accompanying crampy abdominal pains and he noted a fever of 38.2ºC yesterday. He did not note any accompanying weight loss but has been feeling tired over this period.

The abdominal examination was unremarkable. He is not sexually active at present.

He has been hospitalized approximately 5-6 times in the last 3 years with recurrent infections. From his previous medical notes, his last admission related to a chest infection. He had a dry cough and shortness of breath during this time. Oxygen saturation measured on admission was 96% but quickly decreased to 89% on exertion with bilateral opacification noted on chest X-rays.

Stool cultures had been taken and on Ziehl-Neelsen staining, red oocysts are visible within the stool culture. Blood tests taken reveals:

Hb	150 g/L	Male: (135-180)Female: (115 - 160)
Platelets	250 * 10 /L 9	(150 - 400)
WBC	4.5 * 10 /L 9	(4.0 - 11.0)
Neuts	1.1 * 10 /L 9	(2.0 - 7.0)
Lymphs	2.5 * 10 /L 9	(1.0 - 3.5)
Mono	0.6 * 10 /L 9	(0.2 - 0.8)
Eosin	0.3 * 10 /L 9	(0.0 - 0.4)

Immunoglobulin studies were carried out and this revealed reduced levels of IgG and IgA but IgM levels were normal.

What is the most likely unifying diagnosis for his symptoms?

A. Brunton's agammaglobulinemia
B. Chediak-Higashi syndrome
C. Selective IgA deficiency
D. Hyper IgM syndrome
E. Wiskott-Aldrich syndrome

D. Hyper IgM syndrome

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis* pneumonia, hepatitis, diarrhoea

Hyper IgM syndrome is a rare X-linked inherited immunodeficiency that presents with multiple infections throughout their life and typically presents in infancy. It is common to see opportunistic infections as described above as cryptosporidiosis and *Pneumocystis jirovecii* pneumonia. Definitive testing requires flow cytometry to identify the lack of expression of CD40 on T-cells or molecular genetic testing to identify a pathogenic variant on the CD40LG gene. However, findings of neutropenia and reduced IgG and IgA with normal or elevated IgM levels in patients presenting with recurrent, chronic infection highly suggests this diagnosis.

Chediak-Higashi syndrome presents with recurrent infections but this tends to be caused by more common pathogens with recurrent *Staph aureus* being the most common. It is also accompanied by other findings including albinism, photophobia and peripheral neuropathy during teenage years.

Selective IgA deficiency patients tend to be asymptomatic. However, patients can present with recurrent sinopulmonary infections and gastrointestinal infections. It is unlikely in this case due to low IgG levels as selective IgA deficiency will typically have normal IgG levels.

Brunton's agammaglobulinemia will also present with recurrent bacterial infections but investigations will reveal a generalized reduction in all immunoglobulin levels. Definitive tests include genetic testing for mutations within the BTK gene.

Wiskott-Aldrich syndrome typically presents with symptoms bruising and petechiae with eczema during the 1st month of life. Investigations will show thrombocytopenia and immunoglobulin tests will show reduced IgM but elevated IgA and IgE with normal IgG levels. Note that these patients are at increased risk of autoimmune conditions and haematology malignancy.

Question 27 of 89

A 54-year-old woman presents to the emergency department. She has noticed a sore throat over the last 24 hours and checked her temperature and found it to be 38.2ºC. Her other observations are all normal. She has had no other symptoms and specifically denies coughing, chest pain, dysuria and diarrhoea. She is currently undergoing chemotherapy for breast cancer having last had treatment six days ago.

What is the most appropriate treatment?

A. Confirm neutropenia before treatment
B. IV co-amoxiclav and oral clarithromycin
C. Oral metronidazole
D. IV piperacillin with tazobactam
E. IV gentamicin

D. IV piperacillin with tazobactam

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

The correct answer is IV piperacillin with tazobactam. This is a patient who is likely to have a low neutrophil count as she has recently had chemotherapy. Such patients should be treated as neutropenic sepsis if there is a temperature above 38ºC or any other sign of sepsis, and need immediate IV piperacillin with tazobactam. Some units use vancomycin as well at this point. This should be given before confirming the neutropenia as that would cause an unnecessary delay. IV gentamicin would be generally used for pyelonephritis, whilst IV co-amoxiclav and oral clarithromycin would be used for a severe community acquired pneumonia.

Question 28 of 89

A 62-year-old man had a routine set of blood tests performed by his General Practitioner. These demonstrated an erythrocytosis (Packed Cell Volume 0.56) but no other abnormality. Further questioning by the GP found that the patient had no symptoms of hyperviscosity, was a nonsmoker with no symptoms of daytime somnolence and took no regular medications. Past medical history included only a left knee hemiarthroplasty performed due to osteoarthritis.

Two weeks after the initial blood test, the patient's bloods were repeated and showed the persistence of the erythrocytosis. A referral to haematology clinic was made for further investigation. Details of further investigations arranged through haematology clinic are listed below.

Haemoglobin	188 g / L
White cell count	6.7 * 10 /l
Neutrophils	3.2 * 10 /l
Lymphocytes	2.1 * 10 /l
Monocytes	0.8 * 10 /l
Eosinophils	0.3 * 10 /l
Basophils	0.3 * 10 /l
Platelets	202 * 10 /l
Packed cell volume	0.59
Urea	4.5 mmol / L
Creatinine	97 micromol / L
Sodium	140 mmol / L
Potassium	3.9 mmol / L
eGFR	85 ml / min
Ferritin	80 ng / ml
Albumin	38 g / L
Alkaline phosphatase	89 U / L
ALT	25 U / L
Bilirubin	20 micromol / L
JAK 2 V617F mutation	Negative
Serum erythropoietin	0 U / L (reference 0-19)

Blood film: no abnormality detected; no features of myeloproliferative disease Abdominal ultrasound: liver, hepatic duct system and gallbladder unremarkable; mild-moderate splenomegaly; kidneys and renal tract unremarkable

What is the most appropriate next investigation?

A. JAK2 exon 12 mutation testing
B. Bone marrow aspiration and trephine biopsy
C. Measurement of red cell mass
D. CT brain
E. Erythropoietin receptor gene analysis

A. JAK2 exon 12 mutation testing

Erythrocytosis is defined as a haemoglobin > 18.5 g / dL or PCV > 0.52 (male) / 0.48 (female). Patients with a persistent erythrocytosis without a clear cause (i.e. chronic hypoxia or drug causes) should be referred to haematology for further investigation. An urgent referral should be made if symptoms of hyperviscosity or polycythaemia (raised PCV, white cells and platelets) are present.

More than 95 % of individuals with polycythaemia vera test positive for the JAK 2 V617F mutation. Other baseline investigations include a blood film to exclude myeloproliferative disease, renal and liver profiles and serum ferritin (as iron deficiency can mask the degree of erythrocytosis). Abdominal ultrasound is performed in patients with high suspicion for polycythaemia vera as this condition is associated with radiographical splenomegaly in two-thirds of cases.

A low serum erythropoietin is suggestive of primary bone marrow disease even in the absence of JAK 2 mutation and should prompt testing for the rarer exon 12 mutation of JAK 2. This test should be performed before the more invasive bone marrow biopsy.

Raised serum erythropoietin should prompt investigation for an exogenous source, for example, CT brain to look for a cerebellar haemangioma or meningioma.

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A 78-year-old man presents to the acute medical unit with a 3-day history of lower limb weakness. He has a 6-month history of progressive back pain. He denies any bowel or bladder dysfunction, and saddle anaesthesia.

Blood results are as follows:

Hb	110 g/L	Male: (135-180) Female: (115 - 160)
Platelets	182 * 10 /L 9	(150 - 400)
WBC	6.8 * 10 /L 9	(4.0 - 11.0)
Na +	134 mmol/L	(135 - 145)
K +	5.1 mmol/L	(3.5 - 5.0)
Urea	16.2 mmol/L	(2.0 - 7.0)
Creatinine	288 µmol/L	(55 - 120)
Paraprotein	No paraprotein detected	
Kappa free light chains	12,450 mg/L	(3.3 - 19.4)
Lambda free light chains	125 mg/L	(5.7 - 26.3)
Kappa to Lambda ratio	99.6	(0.26 - 1.65)

An MRI spine confirms cauda equina syndrome due to a large paravertebral soft tissue mass. In addition, there is widespread abnormal marrow involvement throughout the spine.

What is the most likely diagnosis?

A. High grade B cell lymphoma
B. Multiple myeloma
C. Prostate carcinoma
D. Solitary bone plasmacytoma
E. Solitary extra medullary plasmacytoma

B. Multiple myeloma

In approximately 1-2% of myeloma cases, the myeloma cells produce very low amounts of paraprotein, which can only be detected using the serum free light chain test. This is called oligosecretory myeloma

The diagnosis is most certainly **multiple myeloma** due to evidence of a monoclonal plasma cell population (markedly raised kappa to lambda ratio) and myelomatous end-organ dysfunction (e.g. anaemia, renal dysfunction and diffuse bone involvement). Although the paraprotein is negative, in approximately 1-2% of myeloma cases, the myeloma cells produce very low amounts of paraprotein, which can only be detected using the highly sensitive serum free light chain test.

Light chains are secreted by B-cells and plasma cells. Individual B- or plasma cells possess either kappa or lambda light chains, but never both together. Interpretation of serum free light chains (sFLC) can be confusing. It is important to remember that it is the ratio that is the most important aspect of the analysis. Several diseases can give rise to increased absolute levels of sFLC. For example due to decreased excretion as seen in renal failure, or due to increased production (e.g. infections, or inflammatory conditions). These 'reactive' causes will result in a broadly similar increase in both kappa and lambda light chains thereby maintaining a normal ratio. However, in monoclonal conditions, the B-cell or plasma cell clone will be either lambda or kappa light chain restricted subsequently resulting in an abnormal ratio.

The large soft tissue mass likely represents an extramedullary plasmacytoma. However, the diagnosis of a **solitary extramedullary plasmacytoma** is excluded given that the patient has myelomatous end-organ dysfunction and involvement of the axial skeleton.

Similarly, a **solitary bone plasmacytoma** is excluded due to the absence of a bone plasmacytoma and the presence of myelomatous end-organ dysfunction.

Although lymphomas can present with soft tissue masses and produce light chains, the clinical features (e.g. anaemia and renal impairment) are more in keeping with myeloma, making a **highgrade B cell lymphoma** less likely.

Prostate carcinoma classically presents with sclerotic bone metastases, and would not cause an abnormal serum free light chain ratio.

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A 72-year-old man attends the emergency department with a headache and blurred vision which has progressively worsened over the past 2 weeks. On examination, his observations are within normal limits, and he has no focal neurology. On fundoscopy, there is bilateral retinal vein dilation and tortuosity with visible retinal haemorrhages.

Blood results are as follows:

Hb	90 g/L	Male: (135-180)Female: (115 - 160)
Platelets	110 * 10 /L 9	(150 - 400)
WBC	4.8 * 10 /L 9	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	10.8 mmol/L	(2.0 - 7.0)
Creatinine	184 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)

Plasma viscosity	4.2mPas	(1.50 -1.72)
IgG	1.2 g/L	(6-16)
IgM	42 g/L	(0.4 - 2.5)
IgA	0.2 g/L	(0.8 - 3.0)

Given the likely diagnosis, what treatment is urgently indicated?

A. Chemotherapy
B. Ibrutinib
C. Plasma exchange
D. Red cell transfusion
E. Steroids

C. Plasma exchange

Patients with Waldenstrom's macroglobulinaemia often present with issues secondary to hyperviscosity

The patient has clinical features of hyperviscosity (e.g. headache, blurred vision, and renal impairment). This is confirmed biochemically with the raised plasma viscosity. The fundoscopic appearances (bilateral retinal vein dilation and tortuosity with retinal haemorrhages) are also classic for hyperviscosity within the retinal vasculature.

The markedly raised IgM level is suggestive of Waldenstrom's macroglobulinaemia.

The presence of anaemia and thrombocytopenia are most likely due to bone marrow infiltration. However alternative causes should also be considered (e.g. autoimmune haemolytic anaemia, and immune thrombocytopenia).

Plasma exchange is correct. Hyperviscosity is a haematological emergency and the patient thus needs emergency plasma exchange. Plasma exchange is an extra-corporeal technique able to remove macromolecules (e.g. IgM) from blood.

Chemotherapy is incorrect. Although the patient will most certainly need chemotherapy to treat their underlying disorder, the first priority is to treat the hyperviscosity by reducing the IgM level with plasma exchange.

Ibrutinib is incorrect. Ibrutinib is a type of tyrosine kinase inhibitor (TKI) that is highly efficacious in a variety of haematological malignancies. It is less toxic compared to traditional chemotherapies and is therefore often used as a first-line agent in frail elderly patients. It can also be used in Waldenstrom's macroglobulinaemia however at the current time the priority is for plasma exchange.

Red cell transfusion is incorrect. Although the patient is anaemic, they most certainly should not receive a red cell transfusion at the current time as this could worsen the hyperviscosity.

Steroids is incorrect. Steroids are often used as chemotherapy adjuncts to treat Waldenstrom's macroglobulinaemia, however at the current time the priority is for plasma exchange.

Question 31 of 89

A 35-year-old woman who was diagnosed with hereditary angioedema is about to undergo an elective meniscal repair for her left knee. She has been well otherwise with no recent changes to her health or medications.

Which is the drug of choice for prophylaxis for her hereditary angioedema prior to her procedure?

A. Prednisolone
B. Hydrocortisone
C. Conestat alfa
D. Tranexamic acid
E. Icatibant

D. Tranexamic acid

The best answer here is tranexamic acid.

In hereditary angioedema, the relevant medications can be used as follows:

A C1-esterase inhibitor can be used for short-term prophylaxis before procedures or to terminate acute attacks of hereditary angioedema. Conestat alfa and icatibant are licensed for the treatment of acute attacks of hereditary angioedema in adults with C1-esterase inhibitor deficiency. Tranexamic acid and danazol are used for short-term and long-term prophylaxis.

There is no role of glucocorticoids in this case

Question 32 of 89

A 65-year-old woman presents to the emergency department with a painful leg. She had noticed that her calf started to become tender when she was getting dressed in the morning and found it to be swollen. She was concerned and called her GP surgery who gave her an emergency appointment. She was seen by her GP earlier in the day who suspected a deep vein thrombosis and advise her to attend her local emergency department.

She has a past medical history of breast cancer which was operated on three months ago with a wide local excision, and she has been told that the operation was successful in removing the cancer. Her observations are stable. On examination, she has a swollen left calf which is mildly tender without erythema. A D-dimer sent by the emergency department team was positive but all other blood tests are normal. She undergoes a doppler ultrasound scan which shows no thrombus.

How should she be further managed?

A. Start warfarin
B. Repeat ultrasound scan within 6-8 days
C. CT pulmonary angiogram
D. Start treatment dose low-molecular weight heparin
E. Repeat D-dimer

B. Repeat ultrasound scan within 6-8 days

The correct answer is to repeat the ultrasound scan within 6-8 days. This is a patient with a major risk factor for deep vein thrombosis (DVT) and pulmonary embolus (PE) who presents with typical features of a DVT; unilateral tender and swollen calf. She would likely have a Well's score at 2 and be considered at high risk.

Since the ultrasound is negative, a repeat ultrasound is advised, and there as of yet no indications to start treatment with either warfarin or heparin. In patients with cancer warfarin is not recommended as treatment for DVT or PE. A CT pulmonary angiogram is not indicated as there are no symptoms or signs suggestive of a

pulmonary embolus. Repeating the D-dimer is unlikely to give any additional information.

'Venous thromboembolic diseases: diagnosis, management and thrombophilia testing' Clinical guideline [CG144]. The National Institute for Health and Care Excellence, June 2012.

Question 33 of 89

A 44-year-old female is referred to haematology outpatients with fatigue, shortness of breath and abnormal blood results organized by her general practitioner. She has no past medical history and is on no medications. She does not smoke or drink alcohol. She works in a bakery.

Clinical examination is unremarkable. Blood tests:

Hb	101 g/L	Male: (135-180)Female: (115 - 160)
Platelets	111 * 10 /L 9	(150 - 400)
WBC	14.2 * 10 /L 9	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	4.1 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)

A blood film is organized, which demonstrates Auer rods. What is the most likely diagnosis?

A. Acute lymphocytic leukaemia
B. Acute promyelocytic leukaemia
C. Chronic lymphocytic leukaemia
D. Chronic myeloid leukaemia
E. Thrombotic thrombocytopenic purpura

B. Acute promyelocytic leukaemia

Auer rods on blood film strongly suggests acute promyelocytic leukaemia

Acute lymphocytic leukaemia is incorrect. Auer rods are not typical of the peripheral blood film in this condition. It may show blast cells in this case or it may be normal if the cells are confined to the bone marrow.

Chronic myeloid leukaemia is incorrect. The blood film in this case would not demonstrate Auer rods but rather a significant leucocytosis consisting of the whole spectrum of mature granulocytes. Organomegaly and lymphadenopathy are common.

Chronic lymphocytic leukaemia is incorrect. This typically affects an older age range with a significant lymphocytosis. The blood film may show 'smear' cells.

Thrombotic thrombocytopenic purpura is incorrect. Clinically this is often characterized by confusion, headache, fever and bruising. It is a medical emergency. The blood film will show schistocytes.

Question 34 of 89

A 58-year-old male is referred to the haematology outpatient department with reports of widespread bruising. He does not have any significant past medical history and does not take any regular medications. He does not smoke or drink alcohol.

On examination, there are widespread ecchymoses affecting all of his limbs, abdomen and thorax. Blood tests:

Hb	111 g/L	Male: (135-180)Female: (115 - 160)
Platelets	167 * 10 /L 9	(150 - 400)
WBC	4.2 * 10 /L 9	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Activated partial thromboplastin time (APTT)	61 seconds	(30-40)
Prothrombin time	11 seconds	(11 - 12.5)
Factor VIII	8 IU/dl	(50-150)
Bleeding time	5 minutes	(3-10)
Lupus anticoagulant	absent	(present)

A mixing study is abnormal and further testing demonstrates the presence of factor VIII inhibitor.

What is the most likely diagnosis?

A. Acquired haemophilia A
B. Haemophilia B
C. Hereditary haemophilia A
D. Vitamin K deficiency
E. Von Willebrand's disease

A. Acquired haemophilia A

Acquired haemophilia A is diagnosed in patients without previous or familial histories of bleeding who have isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity

Acquired haemophilia A is the correct answer. This acquired haemophilia presents in later life without a preceding history of coagulopathy or family history. It is characterised by an isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity. It typically presents with bleeding into the skin or muscles and occasionally haematuria or melena. Haemarthrosis is less likely than with an inherited haemophilia. It is autoimmune disorder with the formation of antibodies that attack clotting factors. A mixing study is crucial in differentiating inherited factor deficiencies from acquired factor deficiencies. In inherited disorders that are characterized by a factor deficiency, the addition of normal plasma to blood restores the clotting parameters. In individuals with a factor inhibitor, the coagulation test remains abnormal.

Haemophilia B is incorrect. This is inherited bleeding disorder characterised by deficiency of factor IX.

Hereditary haemophilia A is incorrect. The absence of a family history, bleeding from a young age and normal mixing study, make this an unlikely diagnosis.

Vitamin K deficiency is incorrect. This will cause an abnormal PT and APTT.

Von Willebrand's disease is incorrect. This will cause an abnormal bleeding time.

Question 35 of 89

A 55-year-old woman is referred to the haematology outpatient department with unexplained eosinophilia. She has a past medical history of systemic lupus erythematosus and recurrent urinary tract infections. Her regular medications include azathioprine and nitrofurantoin.

On examination, there is a rash across the malar region that spares the nasolabial folds but is otherwise unremarkable.

Plain radiography of the chest is unremarkable.

Hb	136 g/L	Male: (135-180)Female: (115 - 160)
Platelets	189 * 10 /L 9	(150 - 400)
WBC	8.2 * 10 /L 9	(4.0 - 11.0)
Neuts	5.2 * 10 /L 9	(2.0 - 7.0)
Lymphs	2.0 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.8 * 10 /L 9	(0.0 - 0.4)

What is the most likely explanation for her eosinophilia?

A. Azathioprine
B. Eosinophilic granulomatosis with polyangiitis
C. Hypereosinophilic syndrome
D. Nitrofurantoin
E. Systemic lupus erythematosus

D. Nitrofurantoin

Nitrofurantoin can cause eosinophilia

Nitrofurantoin is correct. This is an antibiotic used for urinary-tract infections, sometimes given as a prophylactic long-term dose to prevent recurrent infections. It is associated with eosinophilia as a recognised side effect and is the most likely explanation in this case.

Azathioprine is incorrect. Eosinophilia is not a common side effect of this medication. Indeed, it may be used as a steroid-sparing agent in some hyper-eosinophilic syndromes. It is more likely to cause cytopaenias as a side effect.

Eosinophilic granulomatosis with polyangiitis (EGPA) is incorrect. A malar rash is not typical of EGPA but rather of lupus. EGPA typically causes a vasculitic rash, which would be non-blanching and not likely to be located in the malar region. Additionally, there is no history of asthma or sinus problems, making the diagnosis unlikely. Furthermore, the eosinophil count in this disorder tends to be >1.5 * 10 /L.

Hypereosinophilic syndrome is incorrect. This is a myeloproliferative disorder associated with persistent eosinophilia and organ damage. The eosinophil count must be at least 1.5 * 10 /L for this diagnosis to be considered.

Systemic lupus erythematosus (SLE) is incorrect. This disorder is associated with haematological abnormalities. However, active SLE is typically associated with cytopaenias (anaemia, thrombocytopaenia, leucopaenia) rather than the converse. Eosinophilia is not typical

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A 74-year-old patient is referred to the haematology outpatient clinic with a lump in her neck. She has no past medical history.

On examination, widespread lymphadenopathy is detectable in the cervical, inguinal and axillary regions.

Hb	121 g/L	Male: (135-180)Female: (115 - 160)
Platelets	189 * 10 /L 9	(150 - 400)
WBC	95 * 10 /L 9	(4.0 - 11.0)
Neuts	2.0 * 10 /L 9	(2.0 - 7.0)
Lymphs	92.7 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.1 * 10 /L 9	(0.0 - 0.4)

Given the presentation, what is the most important investigation to confirm the diagnosis?

A. Bone marrow aspiration
B. Bone marrow trephine biopsy
C. Cytogenetics
D. Immunophenotyping
E. Labelled white blood cell scan

D. Immunophenotyping

CLL - immunophenotyping is investigation of choice

Immunophenotyping is incorrect. Immunophenotyping by flow cytometry is a method used to detect the presence or absence of white blood cell antigens. These antigens are protein structures associated with white blood cells. Specific groupings of these antigens are normally present on or within white blood cells (WBCs) and are unique to specific cell types and stages of cell maturation. Specific patterns of antigens are present on abnormal cells seen in specific lymphomas like chronic lymphocytic leukaemia (CLL). On flow cytometry, CLL cells classically demonstrate CD5, CD19, CD23, weak monotypic surface immunoglobulin and weak or absent CD79B, CD22 and FMC7.

Bone marrow aspiration is incorrect. A bone marrow aspirate contains a liquid sample from the bone marrow for analysis. Bone marrow (BM) aspirate and trephine biopsy is not typically necessary at diagnosis but is used in cases with atypical features or to rule out differential diagnoses in the case of anaemia/thrombocytopenia.

Bone marrow trephine biopsy is incorrect. A trephine biopsy removes a small piece of bone with the marrow inside. Again, this is not required at diagnosis. Bone marrow trephine biopsies may show interstitial, nodular or diffuse infiltration if carried out.

Cytogenetics is incorrect. This may be used to inform prognosis (as a complex karyotype is associated with poor survival). However, it is not typically required at diagnosis.

Labelled white blood cell scan is incorrect. This scan is typically used to localise a site of unknown infection rather than diagnose CLL

Question 37 of 89

A 44-year-old male presents with a 2-month history of increasing lethargy. His wife reports him to be not quite himself for the past 2 months now, with poor oral intake and poor appetite. He is a self-

employed software engineer but currently is unable to work due to his lethargy. He was previously treated for Hodgkin's lymphoma 5 years ago and has since been in remission.

On examination, he has no conjunctival pallor, is dry on his mucous membranes and extremely lethargic. Firm, rubbery lymph nodes are noted in the right axilla. Cardiovascular examination reveals a soft systolic murmur, respiratory and abdominal examinations are unremarkable. He is a non-smoker and drinks alcohol only occasionally. His blood tests are as follows:

Hb	88 g/l
MCV	104 fl
Platelets	94 * 10 /l9
WBC	12.8 * 10 /l9
Red cell distribution	9% (normal 11.5-14.5%)
Blood film	leucoerythroblastic with myeloblasts

What is the most likely cause of this patient's anaemia?

A. B12 and folate deficiency
B. Iron deficiency
C. Anaemia of chronic disease
D. Myelodysplasia post-chemotherapy
E. Marrow infiltration

A. Marrow infiltration

This patient has a symptomatic macrocytic anaemia, of which B12 and folate deficiency, myelodysplasia post-chemotherapy and marrow infiltration could all be causes. Iron deficiency results in a microcytic anaemia while anaemia of chronic disease typically causes a microcytic or normocytic anaemia. Blood cells in B12 and folate deficiency are typically megaloblastic, large immature red cells caused by impaired DNA synthesis. Myelodysplasia typically results in red cells of abnormal shapes (poikilocytosis) and sizes (anisocytosis) with Pappenheimer bodies (abnormal granules of iron). Chemotherapy is a possible cause of myelodysplasia but typically after recent treatment only. Sadly, in this case, the blood film of myeloblasts and erythroblasts suggests the transformation of Hodgkin's lymphoma into acute myeloid leukaemia, a well-recognised complication of Hodgkin's lymphoma chemotherapy with older alkylating agents, typically 5 to 10 years after treatment. Blast cells have now subsequently infiltrated the bone marrow, resulting in macrocytic anaemia.

Question 38 of 89

A 78-year-old gentleman with chronic lymphocytic leukaemia (CLL) presents with spontaneous bruising. He recalls no trauma and is otherwise well although he takes aspirin, simvastatin and ramipril for a previous myocardial infarction.

On examination, he looks well. His conjunctiva are pale but his chest is clear and he is warm and well perfused. A number of purpura are noted across the arms, back and chest. Palpable lymph nodes are felt in the left inguinal region. There is no hepatosplenomegaly.

Hb	104 g/l	Na +	135 mmol/l
Platelets	54 * 10 /l 9	K +	4.0 mmol/l
WBC	10.3 * 10 /l 9	Urea	3.4 mmol/l
Neuts	6.7 * 10 /l 9	Creatinine	87 µmol/l
Lymphs	3.4 * 10 /l 9	CRP	14 mg/l
Eosin	0.1 * 10 /l9		

What is the most appropriate management option?

A. Suspend aspirin
B. Start chlorambucil
C. Start dexamethasone
D. Platelet transfusion
E. Splenectomy

B. Start chlorambucil

Thrombocytopenia -> indication to start treatment in CLL

This gentleman has developed thrombocytopenia on a background of CLL. This is an indication to start chemotherapy. In some cases, these may also respond to steroids but typically chemotherapy would be started and chlorambucil is a commonly used agent. Suspending aspirin will not fix thrombocytopenia but may be advised. There are no signs of hypersplenism as the cause of the thrombocytopenia. Platelet transfusion will not fix the underlying problem and is not urgent given there is no acute bleeding.

Question 39 of 89

A 30-year-old previously fit and well gentleman is injured following a road traffic accident after being thrown off his motorcycle. He was blue-lighted to the emergency department, where he was found to have multiple, profusely bleeding, lacerations of his extremities.

He was transfused 2 units of cross-matched blood, with no reactions detected in blood bank. Ten minutes after the transfusion, the patient developed severe urticaria.

Which of the following syndromes would contribute to the patient's picture?

A. Adenosine deaminase deficiency
B. Ataxia telangiectasia
C. DiGeorge syndrome
D. Selective IgA deficiency
E. Wiskott-Aldrich syndrome

D. Selective IgA deficiency

IgA deficiency is associated with anaphylactic reaction to blood products

The majority of selective IgA deficiency patients are asymptomatic; with about 5% suffering from recurrent respiratory tract infections. The condition becomes clinically significant when blood transfusion is required, as there is the potential for anaphylaxis to occur on exposure to IgA containing blood products.

Although rare, anaphylaxis can happen from the first transfusion if the patient has been previously exposed to IgA i.e. in consumed animal meat products. If ever the patient needs a future blood transfusion, the transfused blood must be IgA free.

Question 40 of 89

A 16-year-old female was admitted with new onset facial swelling. The facial swelling started 45 minutes ago and initially involved her lips. She complained of a sensation of choking and a feeling of

being unable to speak with hoarseness of her voice. She had been investigated on multiple occasions for abdominal pain and was diagnosed with non-specific abdominal pain. She was not taking any medication and was otherwise healthy prior to the admission.

She was given prednisolone 40mg PO and chlorpheniramine 10mg PO and admitted for observation. Whilst in the department she developed profound shortness of breath with associated stridor. Her swelling around her lips worsened and involved the whole of her face. On examination, she was in respiratory distress with severe biphasic stridor. Her respiratory rate was 32/min with an oxygen saturation of 88% on air. Auscultation of her chest also revealed the presence of a widespread polyphonic wheeze. Examination of her cardiovascular system revealed the presence of flushed peripheries with a bounding peripheral pulse. Her pulse was 102bpm and her blood pressure was 92/68 mmHg. Her GCS was 15 and neurological and abdominal examinations were unremarkable. She was cannulated and commenced on stat intravenous colloid solution. She was given adrenaline 0.5mg IM on three separate occasions within 10 minutes with no improvement. She was transferred immediately to the Intensive Care Unit and an anaesthetist fast bleeped to secure her airway.

What is the best immediate management step pending definitive airway management?

A. Commence IV adrenaline infusion
B. Commence danazol
C. Commence IV dopamine
D. Commence fresh frozen plasma infusion
E. Commence C1 esterase inhibitor concentrate infusion

E. Commence C1 esterase inhibitor concentrate infusion

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

This patient has hereditary angioedema. This condition is characterised by a lack of C1 esterase inhibitor and may present with laryngeal oedema, recurrent abdominal pain and localized subcutaneous swelling. Laryngeal oedema may be fatal, does not respond to glucocorticoids or antihistamines, and has an only modest response to adrenaline. The immediate management is to commence C1 esterase inhibitor concentrate infusion. Fresh frozen plasma infusion may be administered if the concentrate is not available. Danazol is more suitable for subcutaneous oedema or as prophylaxis in certain situations eg prior to surgery.

Question 41 of 89

An 18-year-old woman presents to the emergency department with two weeks of right upper quadrant pain. She also reported longstanding pain in her right femur. She has recently returned from a holiday in Tanzania.

On examination, there was mild tenderness in the right upper quadrant of the abdomen. There was hepatomegaly and splenomegaly detectable along with conjunctival pallor. She is afebrile. There is tenderness over the right femur.

Hb	91 g/L	Male: (135-180)Female: (115 - 160)
Platelets	112 * 10 /L 9	(150 - 400)
WBC	4.2 * 10 /L 9	(4.0 - 11.0)
Na +	138 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	5.3 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	12 µmol/L	(3 - 17)
ALP	88 u/L	(30 - 100)
ALT	32 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	36 g/L	(35 - 50)
LDH	512 U/L	(200-400)
Recticulocytes	43 * 10 /L 3	(5-15)
Direct antiglobulin test	negative	(negative)
Haptoglobin	101 mg/dl	(50-220)

An ultrasound abdomen demonstrates massive splenomegaly (24 x 8 cm) and hepatomegaly. An x-ray of the right femur demonstrates an Erlenmeyer flask deformity.

What is the likely diagnosis?

A. Autoimmune haemolytic anaemia
B. Chronic myeloid leukaemia
C. Gaucher's disease
D. Malaria
E. Myelofibrosis

C. Gaucher's disease

Gaucher disease causes splenomegaly

Gaucher's disease is the correct answer. The patient has hepatomegaly and massive splenomegaly along with anaemia and thrombocytopenia. While all of the options listed can cause splenomegaly, only Gaucher's disease is associated with constriction of the diaphysis and flaring of the metaphysis of the femur, resulting in a deformity known as the Erlenmeyer flask deformity (named because it resembles the conical flask used by chemists).

Autoimmune haemolytic anaemia is incorrect. This is a cause of mild rather than massive splenomegaly. Additionally, the negative direct antiglobulin test and haptoglobin make haemolysis unlikely.

Chronic myeloid leukaemia is incorrect. While this can cause hepatosplenomegaly and cytopenias, it is not associated with characteristic bone abnormalities like Gaucher disease. Additionally, it tends to present in older age rather than childhood/adolescence, like Gaucher's disease.

Malaria is incorrect. While she has travelled recently to Africa, she is afebrile and therefore this diagnosis is very unlikely.

Myelofibrosis is incorrect. This is another cause of massive splenomegaly. However, the characteristic bone abnormality in this condition is osteosclerosis. Additionally, it tends to present after the age of 60.

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A 72-year-old lady is on her third cycle of chemotherapy following mastectomy and axillary clearance of her left breast. She has a PICC line in situ through which she receives her chemotherapy. She developed chills and lethargy two days prior which led her to seek her GP who arranged admission to hospital. She has had one

episode of diarrhoea and is currently being barrier nursed. Her swallowing is a problem due to odynophagia and she is only managing to take oral fluids.

She is currently taking G-CSF, omeprazole and dexamethasone. She has not travelled abroad and reports that she is excluding soft cheeses and pates from her diet.

On exam, she has a clear chest with no murmurs. There is *Candida* in the mouth and a temperature of 38.5ºC recorded on admission. There are no wounds or rashes to be seen. She was started on broad-spectrum intravenous antibiotics and oral nystatin and admitted. You are asked to review her as she has spiked a fever of 39.8ºC on her third day after admission and she is struggling to swallow fluids due to retrosternal pain.

Hb	96 g/l	Na	139 mmol/l
Platelets	123 * 10 /l	K	5.1 mmol/l
WBC	1.6 * 10 /l	Urea	4.5 mmol/l
Neuts	0.5 * 10 /l	Creatinine	56 µmol/l
Lymphs	0.1 * 10 /l	CRP	96 mg/l
Eosin	0.1 * 10 /l		

Chest X-ray	clear lung fields, no effusion, no air under the diaphragm
Bloods cultures (1st peripheral)	no growth
Blood cultures (PICC line)	no growth
Blood cultures (2nd peripheral)	coagulase negative *staphylococcus*
Urine microscopy	no pyuria, no growth
Skin swab (PICC site)	awaited

What of the following is the most appropriate action?

A. Start metronidazole
B. Start fluconazole
C. Take a further set of blood cultures
D. Increase dose of G-CSF
E. Start paracetamol

B. Start fluconazole

Neutropenic sepsis with no response to antibiotics at 48 hrs - > possible fungal infection

This lady has neutropenic sepsis of unknown source and has failed to improve despite broadspectrum antibiotics. This prompts thoughts of what the cause could be. Increasing G-CSF may help her white cells increase but it does not treat the infection present. Paracetamol may reduce fevers but it does not treat the infection. Adding metronidazole is a reasonable thought since it covers anaerobic organisms and she has had a single episode of diarrhoea but the source of the sepsis is not clearly abdominal. Taking two sets of further blood cultures will be part of the workup needed but will not improve the patient's situation. Starting fluconazole is the answer. In any neutropenic sepsis, fungal causes should be considered especially if the patient does not improve on broad spectrum antibiotics. She has oral candida with odynophagia suggests possible oesophageal candidiasis. We should consider this especially given the *Candida* seen.

Question 43 of 89

A 50-year-old woman presents to the emergency department with a 3-day history of headache and blurred vision. Despite taking co-codamol and ibuprofen, her headache has not been relieved and she has since started vomiting. She describes feeling generally unwell for the last 2-3 weeks with general malaise and body aches but denies fever and has no past medical history.

On examination, her visual acuity is reduced with noticeable nystagmus more pronounced on the left side. The remainder of her neurological examination is unremarkable.

Laboratory tests:

Hb	99 g/L	(115 - 160)
Platelets	150 * 10 /L 9	(150 - 400)
WBC	38.3 * 10 /L 9	(4.0 - 11.0)
Lymphs	3.2 * 10 /L 9	(1.0 - 3.5)
Eosin	0.2 * 10 /L 9	(0.0 - 0.4)
Na +	136 mmol/L	(135 - 145)
K +	3.8 mmol/L	(3.5 - 5.0)
Urea	6.2 mmol/L	(2.0 - 7.0)
Creatinine	90 µmol/L	(55 - 120)
Bilirubin	20 µmol/L	(3 - 17)
ALP	87 u/L	(30 - 100)
ALT	39 u/L	(3 - 40)
Albumin	38 g/L	(35 - 50)

What is the most likely diagnosis?

A. Acute myeloid leukaemia
B. Idiopathic intracranial hypertension
C. Meningitis
D. Multiple sclerosis
E. Non-Hodgkin's lymphoma

A. Acute myeloid leukaemia

Acute myeloid leukaemia can present acutely with hyperviscosity syndrome

This patient is presenting with hyperviscosity syndrome. Hyperviscosity syndrome is the increased viscosity of the blood caused by hyperproliferative states (e.g. leukaemia and polycythaemia), increased cell components (e.g. RBCs and WBCs) or increased immunoglobulins (e.g. multiple myeloma). Different bodily systems can be affected, but commonly the central nervous can be affec

ted causing headaches, nystagmus and visual disturbance. This patient's blood results demonstrate a raised WBC count and a normal lymphocyte count, indicating that a large portion of the WBC is made of neutrophils, in keeping with a diagnosis of **acute myeloid leukaemia**. Additional symptoms of acute myeloid leukaemia include lethargy and malaise that are also described by this patient.

Idiopathic intracranial hypertension (IIH) is most common in women and is associated with obesity. It can present with a pressure-type headache with blurred vision. However, eye signs include 6th nerve palsy and papilloedema on fundoscopy. Furthermore, IIH does not explain this patient's raised WBC.

Meningitis can be secondary to a viral or bacterial infection. Presenting features typically include headache, fever and meningism. Vomiting and photophobia may also be seen. Although this patient has a raised WBC that could represent an underlying infection, meningitis does not typically cause nystagmus and the

absence of fever and meningism also suggest an alternative diagnosis.

Multiple sclerosis is a demyelinating disease of the central nervous system. Common presenting symptoms include optic neuritis. Although a patient with multiple sclerosis could present with headache and nystagmus, it does not explain this patient's raised WBC.

Non-Hodgkin's lymphoma is a malignant proliferation of lymphocytes. It can present with malaise and hyperviscosity syndrome as described by this patient. However, additional symptoms include painless lymphadenopathy and constitutional symptoms such as night sweats and weight loss which are not described in this question. Furthermore, the presence of a normal lymphocyte count points towards an alternative diagnosis.

Question 44 of 89

A 44-year-old woman visits her general practitioner with a 10-day history of intermittent epistaxis. She has never had nosebleeds before but now says that even after blowing her nose, it will bleed for 2-3 minutes at a time. There is a past medical history of hypothyroidism for which she takes levothyroxine 75 micrograms daily. Other than recovering from influenza 3 weeks ago, she has had no recent illnesses.

On examination, she is afebrile. Her heart rate is 71bpm and regular with a blood pressure of 125/65mmHg. On auscultation, she has a clear chest with normal heart sounds. Her abdomen is soft and non-tender with no palpable organomegaly. There are multiple bruises and petechiae over her lower limbs and trunk.

Investigations:

Hb	116 g/L	Male: (135-180)Female: (115 - 160)
Platelets	16 * 10 /L 9	(150 - 400)
WBC	5.1 * 10 /L 9	(4.0 - 11.0)
Na +	136 mmol/L	(135 - 145)
K +	3.5 mmol/L	(3.5 - 5.0)
Urea	5.0 mmol/L	(2.0 - 7.0)
Creatinine	61 µmol/L	(55 - 120)
Prothrombin time (PT)	12 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	28 secs	(25-35 secs)
Fibrinogen	2.6 g/L	(2 - 4)
D-Dimer	254 ng/mL	(< 400)

What is the most appropriate next step in this patient's management?

A. Desmopressin
B. Eltrombopag
C. IV immunoglobulin
D. Platelet transfusion
E. Prednisolone

A. Prednisolone

First-line treatment for ITP is oral prednisolone

This patient has immune thrombocytopenic purpura (ITP) the immune-mediated destruction of platelets. In ITP, autoantibodies are directed against glycoprotein IIb/IIIa or Ib-V-IX complexes and can be detected in up to 60-70%. The disease can develop acutely in children following a viral infection or vaccination and usually presents with mucocutaneous bleeding. There is also an association with autoimmune disease. ITP in children is often self-limiting compared to adults which tends to be more of a chronic condition with a relapsing-remitting course. This patient has a history of hypothyroidism and is recovering from a recent viral infection making ITP more likely. Features include easy bruising, epistaxis, purpura and menorrhagia. Massive haemorrhage is a rare complication. The treatment of choice is oral prednisolone at a dose of 1-2mg/kg. Approximately 80% respond to initial treatment.

Desmopressin is used in the treatment of Von-Willebrand's disease (VWD). VWD is a common inherited bleeding disorder that may first present as spontaneous mucocutaneous bleeding. It is caused by a deficiency in the von-Willebrand factor, a protein molecule that encourages platelet adhesion and binds to clotting factor VIII to prevent it from being broken down. A deficiency in this factor predisposes patients to increased bleeding. Blood tests in patients with VWD may demonstrate a microcytic anaemia, thrombocytopenia and a prolonged APTT (especially if factor VIII levels are reduced). However, this patient has never encountered issues with bleeding prior to a recent viral illness. This history combined with an isolated thrombocytopenia makes ITP the more likely diagnosis.

Eltrombopag is a thrombopoietin receptor agonist which acts to increase the platelet count. It is used as a 3rd-line treatment of ITP and is typically prescribed for chronic or refractory ITP.

IV immunoglobulin (IVIG) is another potential treatment option for ITP. It is commonly used in patients who fail to respond to corticosteroids or in patients for which corticosteroids are contraindicated. Another indication for IVIG is if a rapid rise in platelets is needed, for example prior to surgery.

Platelet transfusions are not the treatment of choice in ITP. They are reserved for extreme haemorrhage including intracranial haemorrhage.

Question 45 of 89

A 39-year-old man is referred to the haematology clinic by his GP due to abnormal blood results.

In the clinic, he reports a 2-week history of fatigue, malaise and intermittent abdominal pain. His past medical history includes anxiety and depression for which he takes citalopram. There is no history of smoking or recreational drug use although he drinks 6 cans of cider most evenings. He returned from a trip to India last month.

On examination, he appears lethargic. Chest auscultation is clear and his abdomen is soft with generalised tenderness.

Repeat blood tests are requested:

Hb	100 g/L	(135-180)
Mean Cell Volume	105 fL	(80 - 100)
Platelets	100 * 10 /L 9	(150 - 400)
WBC	7.1 * 10 /L 9	(4.0 - 11.0)
Bilirubin	80 µmol/L	(3 - 17)
ALP	118 u/L	(30 - 100)
ALT	40 u/L	(0 - 40)
AST	65 u/L	(< 35)

Blood glucose	6.1 mmol/L	(4 - 7)
Total cholesterol	7.3 mmol/L	(< 5)

Further investigations are sent:

Blood film	Schistocytes
Coombs test	Negative

What is the most appropriate management for this patient?

A. Alcohol cessation
B. Artesunate
C. Blood transfusion
D. Intravenous immunoglobulin (IVIg)
E. Prednisolone

A. Alcohol cessation

Zieve syndrome usually resolves with abstinence from alcohol

Alcohol cessation is correct. This patient has a likely diagnosis of Zieve syndrome given the triad of non-autoimmune haemolysis, jaundice and hyperlipidaemia on a background of alcohol excess. The negative Coombs test indicates non-autoimmune haemolytic anaemia. In Zieve syndrome, jaundice can be cholestatic in nature but also secondary to haemolysis. The raised ALP supports a cholestatic picture. Zieve syndrome is a rare syndrome and generally resolves following the cessation of alcohol use.

Artesunate is incorrect. Another differential diagnosis for haemolytic anaemia includes infective causes such as malaria. Although this patient has recently travelled to India, the majority of India is relatively malaria-free in comparison to other parts of the world. It also does not account for the raised triglyceride level and cholestatic jaundice.

Blood transfusion is incorrect. Generally, the threshold for blood transfusion is a Hb < 70g/dL or < 80g/dL if the patient has ischaemic heart disease. It would not treat this patient's underlying diagnosis.

Intravenous immunoglobulin (IVIg) is incorrect. This can be used to treat autoimmune haemolytic anaemia and other haematological conditions such as immune thrombocytopenic purpura. However, the negative Coombs test makes autoimmune haemolytic anaemia highly unlikely.

Prednisolone is incorrect. Like IVIg, prednisolone is used in the treatment of autoimmune haemolytic anaemia. This is unlikely to be the underlying diagnosis since the Coombs test is negative. Therefore, other causes of haemolytic anaemia should be considered and investigated

Question 46 of 89

A 59-year-old man suddenly becomes unwell on the oncology unit. He is receiving an intravenous infusion of a new chemotherapy agent as part of a clinic trial. He says he feels very lightheaded. On examination his blood pressure is 80/50 mmHg, heart rate is 120/min, oxygen saturations are 94% on air and bilateral wheeze is heard on auscultation of the chest. An ECG shows a sinus tachycardia of 120 beats per minute. The infusion is stopped, the patient is lay flat with their legs raised and an arrest call has been put out.

What should you administer immediately?

A. 0.5mL of 1:1000 intramuscular adrenaline
B. 0.5mL of 1:10000 intramuscular adrenaline
C. 0.5mL of 1:1000 intravenous adrenaline
D. 0.5mL of 1:10000 intravenous adrenaline
E. 1mL of 1:10000 intravenous adrenaline

A. 0.5mL of 1:1000 intramuscular adrenaline

Anaphylaxis - adult adrenaline dose = 500 mcg (0.5 ml of 1 in 1,000)

This patient is having an anaphylactic reaction to the infusion. Essential immediate management of anaphylaxis comprises: recognition that the patient is seriously unwell, removal of the trigger (if possible), an early call for help, assessment via the ABCDE (airway, breathing, circulation, disability, exposure) approach and administration of adrenaline.

The correct dose of adrenaline in anaphylaxis via the intramuscular route is 0.5mL of 1:1000 (1mg in 1mL/ 0.5mg in 0.5mL). Adrenaline should usually be administered via the intramuscular route as there is a lower risk of inappropriate administration, the incidence of adverse effects is rare, it is an easy method to learn and IV access is not required. Inappropriate intravenous administration risks precipitating arrhythmias, which may result in cardiac arrest. Specialists such as anaesthetists may use the intravenous route, but for the majority of practitioners the intramuscular route is the best option.

As soon as possible after or concurrently with the administration of adrenaline; high-flow oxygen and a rapid intravenous fluid challenge should be delivered. Subsequent to this, an intravenous or intramuscular antihistamine (e.g. chlorphenamine) and steroid (e.g. hydrocortisone) may be given.

Question 47 of 89

A 24-year-old male is admitted with shortness of breath. On examination his respiratory rate is 34 breaths per minute and heart rate is 125 beats per minute. His blood pressure is 120/85 mmHg. An SpO2 reading is 84%. He looks cyanotic. He has a past medical history of coeliac disease, dermatitis herpetiformis, rheumatoid arthritis and asthma. His regular medicines include dapsone, prednisolone, paracetamol and ibuprofen. He just recently completed a course of amoxicillin for a chest infection.

An arterial blood gas is performed (on 15 litres of O2):

Hb	125 g/l
pH	7.33
PaO2	58.11 kPa
PaCO2	2.48 kPa
SO2	99.7%
HCO3	12 mmol/l

What drugs is most likely implicated?

A. Dapsone
B. Amoxicillin
C. Prednisolone
D. Ibuprofen
E. Paracetamol

A. Dapsone

Dapsone + dyspnoea → methaemoglobinaemia

Several inferences should be made with regards to the blood gas. The PaO2 is appropriately high given the patient is on 15L of O2. A simple way of estimating an appropriate PaO2 is to multiple the % of inspired O2 (FiO2) by 2/3. For example, 15L of O2 driven by a non-rebreather mask delivers approximately 90% of O2. Therefore we would expect the PaO2 to be is approximately 2/3 * 90 = 60 kPa. The patient in this example has a PaO2 of 62.22 kPa. Therefore we can confidently state that gas exchange at the level of the alveoli is not the cause of the cyanosis. It is important toremember that the PaO2 is a measure of dissolved O2 in blood. Oxygen is carried in the blood in two forms: dissolved in plasma (about 2% of the total) and reversibly bound to haemoglobin (about 98% of the total). Therefore alternative causes for the cyanosis should be sought e.g. anaemia, shock, and toxic causes (e.g. methemoglobinemia).

The saturation of Hb on the ABG (SaO2) is 99.7%. This is strange as there is a large discrepancy between this and the peripheral pulse oximeter result (86%). This should alert you to consider two differentials - carbon monoxide poisoning and methemoglobinemia. The SaO2 on the blood gas machine is broken down to several components - O2Hb (the 'true' saturation of Hb with O2), COHb (carboxyhemoglobin), HHb, and MetHb. The sum of all these components produces the total saturation SaO2. In this case, the patient has a significantly high MetHb confirming the diagnosis of methemoglobinemia. The true oxygen saturation is 55.3%. This is the cause of the hypoxia and the resultant lactic acidosis.

Methemoglobinemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left. This results in tissue hypoxia. Drugs (e.g. sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine) are common causes. Dapsone is a common cause of methemoglobinemia.

None of the other agents are known to cause methemoglobinemia.

Question 48 of 89

A 64-year-old man presents to the haematology clinic with a history of back pain over the past 6 months. On systematic enquiry and examination, there are no features of spinal cord compression or cauda equina syndrome.

Blood results are as follows:

Hb	110 g/L	Male: (135-180)Female: (115 - 160)
Platelets	165 * 10 /L 9	(150 - 400)
WBC	6.2 * 10 /L 9	(4.0 - 11.0)
Na +	135 mmol/L	(135 - 145)
K +	4.8 mmol/L	(3.5 - 5.0)
Urea	10.8 mmol/L	(2.0 - 7.0)
Creatinine	190 µmol/L	(55 - 120)
Protein electrophoresis	Monoclonal IgG 38g/l	

Given the likely diagnosis, what is the imaging modality of choice?

A. CT PET
B. No imaging required
C. Plain film skeletal survey
D. Whole body MRI
E. Whole body low-dose CT

D. Whole body MRI

Whole body MRI 1st line imaging in suspected multiple myeloma

The clinical features (e.g. back pain, anaemia, renal dysfunction), and the presence of a paraprotein make multiple myeloma the most likely diagnosis.

Whole body MRI is recommended as the first-line imaging modality in multiple myeloma. MRI is the most sensitive tool available for detecting marrow infiltration at an early stage, before bone destruction occurs, as well as offering improved detection of lesions, particularly in the axial skeleton.

Skeletal survey is incorrect. The major disadvantage of plain X-rays is the significantly lower sensitivity compared to advanced imaging. Lytic lesions are only demonstrated when at least 30-50% of the trabecular bone has been lost and around 20% of myeloma patients have no abnormal findings by plain X-ray. Plain X-rays cannot distinguish osteopenia or vertebral collapse caused by myeloma from more common causes such as early osteoporosis or corticosteroid use. For these reasons - skeletal surveys with plain X-rays are no longer recommended.

CT skeletal survey is incorrect. From a practical point of view, CT has the advantage of being quick to perform and allows patients to lie on their back, without the need to change position. CT is also helpful for visualising soft tissue involvement, assessing spinal fracture stability, depicting spinal cord and cauda equina compression (although MRI is superior for this), guiding needle biopsies and surgical interventions, and planning radiotherapy. However, MRI remains the gold standard.

FDG PET/CT is incorrect. PET may be considered for patients with newly diagnosed nonsecretory or oligosecretory myeloma and for evaluation of extramedullary disease. Although FDG PET/CT has some prognostic value when used in the initial diagnosis of myeloma, there is currently insufficient evidence to justify the routine use of FDG PET/CT in all cases of newly diagnosed myeloma.

No imaging required is incorrect. The patient most certainly has a new diagnosis of multiple myeloma and thus cross-sectional imaging is required.

Question 49 of 89

A 22-year-old man is seen in the general medical clinic. He has had several episodes of gallstones over the last three months. He is due to see the surgical team for consideration of laparoscopic cholecystectomy but he was also referred to the medical team due to anaemia. He has needed blood transfusions in the past when he has become tired and found to be anaemic. He was referred for an appointment with a haematologist but was unable to attend and therefore discharged from the clinic without seeing the consultant. He takes no regular tablets. He is unaware of any family history of significant medical problems, but does think that his mother used to turn yellow when slightly unwell, but thinks that this has never been a serious medical problem. He also knows that his father, to whom he is estranged, had some medical problem with his blood. His observations are normal as is his examination apart from conjunctival pallor and 2cm of a palpable spleen.

Blood tests:

Hb	110 g/l
MCV	84.1 fl
MCHC (mean corpuscular haemoglobin concentration)	391 g/l
Platelets	389 * 10 /l9
WBC	8.2 * 10 /l9
Na +	138 mmol/l
K +	4.8 mmol/l
Urea	5.2 mmol/l
Creatinine	85 µmol/l
Bilirubin	22 µmol/l
ALP	42 u/l
ALT	15 u/l

What is the most likely underlying diagnosis?

A. Sickle cell disease
B. Pernicious anaemia
C. Glucose-6-phosphate dehydrogenase (G6PD) deficiency
D. Thalassaemia
E. Hereditary spherocytosis

A. Hereditary spherocytosis

Hereditary spherocytosis is an explanation for anaemia in recurrent gallstones

This young man has a history of anaemia with recurrent gallstones. This implies that there has been destruction of red blood cells and the subsequent rise in bilirubin has provoked the formation of gallstones. The presence of normocytic anaemia with elevated MCHC further supports a diagnosis of spherocytosis. The family history of potentially Gilbert's syndrome would raise the possibility of the patient having this diagnosis as well, which would increase the possibility of gallstones in spherocytosis. The presence of splenomegaly supports this diagnosis. Diagnosis would be confirmed with microscopy and osmotic fragility testing. Pernicious anaemia would be macrocytic and would not be associated with haemolysis. Sickle cell disease would clinically have severe haemolytic normocytic anaemia, recurrent infections and vaso-occlusive phenomena. The absence of such episodes and age of presentation makes sickle cell disease unlikely. In addition, it is screened for in the UK and routinely diagnosed in the neonatal setting. G6PD is a X-linked cause of haemolytic anaemia triggered commonly by drugs causing acute episodes of haemolysis. The absence of a neonatal history of jaundice and demographic risk factors, as well as no trigger makes this less likely, as does the presence of splenomegaly. Thalassaemia would not cause splenomegaly or gallstones

Question 50 of 89

A 32-year-old woman is on her second cycle of chemotherapy for breast cancer. She has developed two days of watery diarrhoea and vomiting. She has occasional chills and feels generally weak. She has not travelled abroad and there are no ill contacts. Her husband is a farmer and together they attended a farm foods show which hosted local cheese and meats in the local region.

On examination, she has a soft abdomen that is mildly tender in the right iliac fossa. Her mucosa is dry and she is achy in muscle groups throughout her body.

Hb	110 g/l	Na +	138 mmol/l
Platelets	348 * 10 /l 9	K +	3.9 mmol/l
WBC	2.4 * 10 /l 9	Urea	4.3 mmol/l
Neuts	0.7 * 10 /l 9	Creatinine	76 µmol/l
Lymphs	1.4 * 10 /l 9	CRP	96 mg/l
Stool specimen	gram-positive bacillus		

What is the causative organism in this case?

A. Listeriosis
B. Salmonellosis
C. Shigellosis
D. Clostridium perfringens poisoning
E. Staphylococcus aureus poisoning

A. Listeriosis

Neutropenic patients should avoid soft cheese due to risk of listeriosis

This is a case of neutropenic sepsis. Patients are at high risk to many organisms and it is suggested they avoid cold meats and dairy products. She had gastrointestinal symptoms and cultured a gram-positive bacillus. This immediately rules out salmonellosis and shigellosis. The gram-positive is a bacillus so cannot be *staphylococcus*. Of the two remaining, only *listeria* is found in dairy products and therefore is the likely cause of her illness

Question 51 of 89

A 22-year-old woman awaiting stem cell transplant for acute myeloid leukaemia has become unwell over the past three days and arrives with a Glasgow Coma Scale of 3 in the emergency department. Her boyfriend who is present with her reports that she has had severe headaches and been sitting in bed but gradually became more confused. She was struggling to breathe and began to seize causing him to call the ambulance.

On examination, she is intubated and has bilateral coarse crepitations. Her pupils are reactive but she is sedated and does not respond to pain. There is papilloedema bilaterally and haemorrhages are seen in the left eye. She is warm and well perfused but her left arm is cold and pale. She is transferred to the intensive care unit.

Hb	120 g/l
Platelets	350 * 10 /l9
WBC	105 * 10 /l9
Troponin	10,876 (normal range <20)
CRP	56 mg/l
Chest x-ray	bilateral pulmonary infiltrates, small left sided effusion

What medical treatment will correct her underlying pathology should be initiated?

A. Intravenous antibiotics
B. High dose corticosteroids
C. Leukapheresis
D. High dose chemotherapy
E. Venesection

C. Leukapheresis

Leukapheresis can be used to acutely lower the white cell count in AML

This lady presents with pulmonary oedema and neurological dysfunction on a background of hyperleukocytosis. This is leukostasis where the blood is thick in white cells. The treatment is to rapidly remove white cells. This can be done by leukapheresis of the blood and removing the white cells which is called leukapheresis and this is the most appropriate answer. Venesection and high dose chemotherapy are less effective ways of achieving a lower white cell count.

Corticosteroids and antibiotics will not help.

Question 52 of 89

A 64-year-old woman is referred by her GP to the haematology clinic with an incidental lymphocytosis noted first four months prior. On questioning, she reports that she has been feeling more fatigued over the past few months and has begun to experience episodes of early satiety, both of which she attributed to looking after her two grandchildren. She is otherwise well and denies any fevers, night sweats or unusual bruising.

On examination, she is slim with an unremarkable cardiovascular and respiratory exam. There is a fullness in the left upper quadrant which moves with inspiration but no lymphadenopathy.

Her blood tests are shown below:

Hb	140 g/L	Male: (135-180)Female: (115 - 160)
Platelets	200 * 10 /L 9	(150 - 400)
WBC	30.1 * 10 /L 9	(4.0 - 11.0)
Neuts	4.0 * 10 /L 9	(2.0 - 7.0)
Lymphs	25.0 * 10 /L 9	(1.0 - 3.5)
Mono	0.8 * 10 /L 9	(0.2 - 0.8)
Eosin	0.3 * 10 /L 9	(0.0 - 0.4)
Blood Film	lymphocytosis with smudge cells	

Ultrasound abdomen confirms splenomegaly.

Chromosomal analysis is performed to guide further management.

Given the likely diagnosis, which of the following chromosomal findings would suggest a poor prognosis?

A. >2% mutation immunoglobulin heavy chain variable region
B. Deletion of 13q
C. Deletion of 17p
D. < 20% CD38 expression
E. TP53 - wild-type

C. Deletion of 17p

del 17p is associated with a poor prognosis in CLL

This patient has chronic lymphocytic leukaemia (CLL) demonstrated by a history of significant lymphocytosis for > 3 months and splenomegaly with a blood firm showing smudge cells. A bone marrow aspirate is not required in all CLL patients but may be indicated in patients with anaemia and/thrombocytopenia to confirm whether these may be attributed to marrow infiltration or splenic destruction.

The deletion of 17p is associated with a poor prognosis in CLL. All other options are markers of good prognosis. Note that a wild type TP53 refers to an unmutated form, however, a mutated TP53 is, by contrast, a bad prognostic marker.

Question 53 of 89

A 54-year-old alcoholic man with chronic hepatitis C is taken to the emergency department by the police. There it was noted that the man had blisters and crusted lesions on his face and lower arms.

Laboratory tests showed elevated plasma porphyrins and elevated uroporphyrin I in the urine, and isocoproporphyrin in the faeces. Biopsy of the skin lesion showed subepidermal blisters with minimal inflammation, marked solar elastosis, thickening of the vessel wall in the papillary dermis and 'caterpillar bodies' in the roof of the blister.

Which of the following is the most likely diagnosis?

A. Acute intermittent porphyria
B. Delta-aminolevulinic acid dehydrase deficiency
C. Erythropoietic protoporphyria
D. Hereditary coproporphyria
E. Porphyria cutanea tarda

A. Porphyria cutanea tarda

Porphyria cutanea tarda causes chronic blistering and crusting skin lesions on sun-exposed skin. Precipitating factors: iron (even if normal amounts), oestrogen and alcohol use, and chronic hepatitis C infection.

The findings on skin biopsy can help with the diagnosis but are not very specific (the 'caterpillar bodies' are essentially clumps of basement membrane material). The key to the diagnosis is the presentation and porphyrin analysis

Question 54 of 89

A 68-year-old female, presents with lethargy and anorexia. She underwent a partial gastrectomy 3 years ago for bleeding gastric ulcer. Her blood results showed:

Hb	90 g/l
MCV	109 fL
Platelets	60 * 10 /l9
WBC	3.5 * 10 /l9
Blood film	Oval erythrocytes, macrocytic erythrocytes, hypersegmented neutrophils, low platelets and basophilic stippling

What is the underlying diagnosis?

A. Sideroblast anaemia
B. Spur cell haemolysis
C. Vitamin-B12 deficiency
D. Thalassaemia
E. Myelodysplasia

C. Vitamin-B12 deficiency

Gastrectomy is defined as partial when a part of the stomach is removed surgically and as total when the entire stomach is

removed. Typical indications are gastric cancer, recurrent gastric ulcers, large duodenal perforations, bleeding gastric ulcers and gastrointestinal stromal tumours. Malnutrition is less common after partial than after total gastrectomy, but the key nutritional deficiencies are iron-deficiency anaemia, calcium deficiency, and vitamin B12 deficiency. However, the hypersegmented neutrophils are strongly suggestive of B12 deficiency.

Hypersegmented neutrophils are hallmarks of B12 deficiency in multiple choice questions

Question 55 of 89

A 19-year-old man is referred to see you as he has been suffering from recurrent epistaxis and he tells you that if he accidentally injures himself the wound bleeds for a long time.

Initial blood tests are as follows:

Hb	101 g/l
MCV	79 fl
Platelets	298 * 10 /l9
WBC	9.2 * 10 /l9
Bleeding time	Prolonged
PT	14 seconds
APTT	28 seconds
LDH	290 u/l (240 - 480 u/L)
Factor VIIIc	low
Ristocetin platelet aggregation test	Impaired aggregation

What is the single most likely diagnosis?

A. Haemophilia A
B. Haemophilia B
C. Haemophilia C
D. Idiopathic Thrombocytopenic Purpura (ITP)
E. von Willebrand's disease

A. von Willebrand's disease

This patient has a coagulopathy and normal platelets, which immediately excludes ITP. Factor VIIIc is low, meaning that the diagnosis must either be haemophilia A or von Willebrand's disease. In this patient two things favour the diagnosis of von Willebrand's over haemophilia A. Firstly, the bleeding time is prolonged and secondly, the platelet aggregation is impaired in response to ristocetin. Both of these would be normal in haemophilia.

question 56 of 89

A 21-year-old girl complains of easy bruising. She has menorrhagia for which she is being investigated by the gynaecology team. She takes no regular medications. Her father had prolonged bleeding after a tooth extraction.

Blood tests show:

Hb	110 g/L
MCV	74 fL
WBC	4.2 x 10^9/L
Platelets	135 x 10^9/L
APTT	45 seconds
INR	1.0

What is the most likely diagnosis?

A. Haemophilia B
B. Anti-thrombin III deficiency
C. Von Willebrand's disease
D. Immune thrombocytopenia
E. Haemophilia A carrier

C. Von Willebrand's disease

Von-Willebrand's disease is an autosomal dominant condition (chromosome 12) that leads to a mild-moderate bleeding tendency. The prevalence of clinically significant cases is 1 in 10,000. Factor VIII is bound to vWF, which protects it from breakdown, so deficiency of vWF can lead to low factor VIII levels and a prolonged APTT. In this case the patient also has a microcytic anaemia, which would be in keeping with iron deficiency anaemia secondary to menorrhagia. Haemophilia B (Factor IX deficiency) is X-linked so does not affect females. Haemophilia A (Factor VIII deficiency) is also X-linked. Most carriers are asymptomatic. The APTT is normal in ITP. Anti thrombin III deficiency is a pro thrombotic condition.

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A 72-year-old woman with breast cancer presents with a swollen, painful left calf. She is known to have metastases in the vertebral bodies and is taking denosumab as prophylaxis. A Doppler ultrasound is arranged which shows a proximal deep vein thrombosis on the left side. This is her first episode of venous thromboembolism.

What is the most appropriate management?

A. Warfarin for 3 months
B. Warfarin for 6 months
C. Low-molecular weight heparin for 3-6 months
D. Direct oral anticoagulants (DOACs) for 3-6 months
E. Aspirin 300 mg for 3 months

C. Low-molecular weight heparin for 3-6 months

Cancer patients with VTE - 6 months of a DOAC

Question 58 of 89

A 23-year-old gentleman reviewed by the on-call medical team after having become unwell in the radiology department. He was undergoing a contrast-enhanced MRI of the small bowel to investigate ongoing diarrhoea. He has no other past medical history and takes no regular medications. He is not known to have any allergies.

Ten minutes ago he started feeling his throat closing up and became very anxious. This was shortly after having been given a contrast agent by IV injection. The medical emergency team arrives quickly and note him to be tachycardia at 132/min and hypotensive with a blood pressure of 82/35mmHg. He also has a widespread erythematous rash over his body and feels itchy. He is treated for anaphylactic shock.

Which blood tests could confirm anaphylaxis?

A. Histamine levels

B. Mast cell tryptase immediately and repeat within one to two hours
C. Mast cell tryptase immediately and repeat within 12 hours
D. Mast cell tryptase immediately and repeat within 24 hours
E. Serum immunoglobulins

B. Mast cell tryptase immediately and repeat within one to two hours

Anaphylaxis - serum tryptase levels rise following an acute episode

The correct answer is mast cell tryptase immediately and repeat within one to two hours. Tryptase levels are the most specific marker for an anaphylactic reaction. Tryptase is a marker of mast cell activation. Serum concentration is normally very low and will quickly return to normal, which is why an immediate sample can be useful but should never delay treatment. Tryptase levels increase to maximum levels over 30 minutes from the onset of symptoms, then peaks at one to two hours. The half-life of tryptase is roughly two hours and may return to normal within six to eight hours. This means that a sample at 12 or 24 hours may not confirm anaphylaxis. Histamine levels can be elevated in various conditions, including simple allergic reactions and does not help to distinguish anaphylaxis. Immunoglobulins are elevated in cell-mediated immune responses.

Question 59 of 89

A 43 year old man is brought to the Emergency Department by his wife. She has become worried about him in the past six months as he has become increasingly confused, aggressive and depressed. He has also lost 4kg in weight in this time and has developed severe, intermittent abdominal pain and diarrhoea, and complains of constant headaches.

Examination reveals a normal cardiorespiratory examination but the abdomen is diffusely tender and there is tender fullness in the right upper quadrant. Neurological examination reveals minor hypotonia throughout and there are bilateral radial nerve palsies as well as a left common peroneal nerve palsy. Sensation appears intact. He is alert but confused with an abbreviated mental test score of 7/10.

Blood tests reveal:

Sodium	136mmol/L	ALP 135U/L Haemoglobin 79g/L
Potassium	5.1mmol/L	AST 265U/L MCV 101fL
Urea	7.1mmol/L	ALT 298U/L White cells 9.4x10^9/L
Creatinine	102µmol/L	GGT 197U/L Neutrophils 5.6x10^9/L
CRP	10mg/L	Bilirubin 12µmol/L Lymphocytes 3.1x10^9/L
Calcium (corr)	2.34mmol/L	Eosinophils 0.1x10^9/L
Phosphate	0.56mmol/L	Basophils 0.6x10^9/L
Magnesium	0.76mmol/L	
Glucose	3.8mmol/L	

The blood film shows anaemia with a dimorphic picture, significant reticulocytosis and high basophil numbers with cytoplasmic stippling.

The patients wife tells you all the symptoms coincided with the patient starting a new job as a loading crane driver at a scrap-yard.

What is the most likely diagnosis?

A. Chronic alcoholism
B. Acute promyelocytic leukaemia
C. Porphyria cutanea tarda
D. Chronic lead poisoning
E. Minimata disease

D. Chronic lead poisoning

Abdominal pain, constipation, neuropsychiatric features, basophilic stippling → lead poisoning

The above vignette gives a classical description of chronic lead poisoning, also known as plumbism or Devon colic. The typical signs are gastrointestinal and neuropsychiatric and include severe, colicky abdominal pain with weight loss and diarrhoea and a metallic taste in the mouth. Insidious neurological signs include headache, difficulty concentrating, subtle personality changes including aggression and difficulty sleeping, dyspraxia and cerebellar signs. The pathognomonic hallmark of chronic lead poisoning is a radial nerve palsy, or wrist drop, although many peripheral nerve palsies may be seen. Patients may also have a bluish discolouration to their skin and a blue line on the gums, known as Burtons line, is very rarely seen. Biochemically, a hepatitic picture can be seen and also occasionally renal impairment due to proximal renal tubular failure, particularly with increased excretion of phosphate and glucose and acidification of the urine. However, most notable is the haematological impact of lead poisoning with a pronounced anaemia, often with dimorphic picture and reticulocytosis due to arrest of the haem biosynthetic pathway. Basophilia with stippling is seen and bone marrow trephine may show ring sideroblasts.

Blood lead levels do not correlate well with total lead burden and the diagnosis may be missed due to incorrect assay or test selection. Since lead is concentrated in red cells, whole blood levels of lead rather than plasma must be analysed, however testing for enzymes affected by lead is more reliable than whole lead levels alone, and hence erythrocyte zinc protoporphyrin (ZPP) levels and delta aminolevulinic acid dehydratase (ALAD) are more reliable. These, coupled with skeletal analysis and blood lead levels are used to test for occupational lead poisoning. The term metal fume fever is used to describe many syndromes of heavy metal and metal oxide poisonings, often in gantry crane drivers who deposit scrap metals in furnaces from above. Many scrap metals are coated in lead based paints leading to occupational lead toxicity syndromes.

Lead poisoning is clinically similar to porphyria and pathologically an interruption in haem pathways are seen in both. The classical hallmark of porphyria cutanea tarda is a blistering photosensitive rash that is not present in this case. Chronic alcoholism may cause B12 deficiency and hence a megaloblastic anaemia and confusion but it is unlikely to cause this constellation of neuropathies and does not explain the basophilic stippling. There is no mention of the patients alcohol habits either. An acute promyelocytic leukaemia presents with non specific symptoms and infections. It may present with sudden onset neurological symptoms only if there is a spontaneous intracranial bleed, in which case the outlook is bleak. It is unlikely here. Minimata disease is an acute mercury toxicity and presents with neuropsychiatric symptoms and rapid

death. It would not be expected to cause the haematological picture seen here.

Question 60 of 89

A 30-year-old man with acute myeloid leukaemia receives a bone marrow transplant from a matched unrelated donor.

7 days post-transplant, he develops a non-blanching purpuric rash over both legs. The rash is not itchy or scaly.

His heart rate 98/min and his blood pressure is 124/72 mmHg. His temperature is 37.3 ºC and he is otherwise asymptomatic.

Blood tests are as follows:

Hb	89 g/l	Na +	138 mmol/l
Platelets	9 * 10 /l 9	K +	3.2 mmol/l
WBC	0.8 * 10 /l 9	Urea	4 mmol/l
Neuts	0.2 * 10 /l 9	Creatinine	62 µmol/l
CRP	10 mg/ll		

What is the most likely cause for the rash?

A. Fungal infection
B. Graft vs host disease
C. Henoch Schonlein purpura
D. Meningitis
E. Thrombocytopenia

E. Thrombocytopenia

This man is on day 7 of his transplant and his blood counts are starting to drop, including his platelets. Thrombocytopenia typically causes small purpuric spots that are otherwise asymptomatic.

A fungal infection is possible in an immunosuppressed patient but would be more likely to cause an itchey or painful rash with a different appearance.

Graft vs host disease typical causes a dry scaley rash and develops when the patients immune system is starting to recover, around 2 weeks after transplant. Henoch Schonlein purpura typically affects children and is associated with a glomerulonephritis. It is immune mediated so unlikely in someone who is still profoundly immunosuppressed.

Meningitis can cause a non-blanching purpuric rash but the patient would be symptomatic with headache, fever, meningism and a CRP rise.

Question 61 of 89

A 45-year-old woman is admitted with chest pain three days after binge drinking 4 bottles of wine and 250mL of spirits.

She has a background of alcohol excess and systemic lupus erythematosus. She has a family history of G6PD deficiency on her father's side.

On examination, she is hemodynamically stable but jaundiced. She has pain on palpation over her right upper quadrant. Chest is clear and heart sounds are normal.

Hb	67 g/L	Male: (135-180)Female: (115 - 160)
Platelets	130 * 10 /L 9	(150 - 400)
WBC	9.8 * 10 /L 9	(4.0 - 11.0)
Bilirubin	72 µmol/L	(3 - 17)
ALP	360 u/L	(30 - 100)
ALT	70 u/L	(3 - 40)
Amylase	67 u/L	(40-140)
Triglycerides	5.8 mmol/L	(<1.7)
LDH	1095 IU/L	(105-333)
Direct anti-globulin test	Negative	

Spur cells and acanthocytes are present on blood film.

Given the likely diagnosis, what treatment from the following options would be most appropriate?

A. Abstinence from alcohol
B. Ascorbic acid
C. Intravenous fluids
D. Liver transplantation
E. Oral prednisolone

A. Abstinence from alcohol

Zieve syndrome usually resolves with abstinence from alcohol

This patient is presenting with jaundice, hyper-triglyceridaemia, and Coomb's negative haemolytic anaemia due to alcoholism and recent binge. The diagnosis here is Zieve syndrome - a rare complication of alcohol excess that is thought to be caused by changes in the red cell membrane due to the transient hyperlipidaemia seen following alcohol binges.

Abstinence from alcohol is the correct answer. Treatment of Zieve syndrome is with supportive management with blood transfusion and abstinence from alcohol. In rare cases, plasmapheresis may be required.

Ascorbic acid is incorrect. This can be used in the treatment of G6PD deficiency, however, this patient does not have this condition. G6PD is inherited in an X-linked recessive pattern and so a female child of a male with G6PD deficiency would be a carrier. G6PD deficiency would also not explain the cholestatic liver function tests and rise in triglycerides.

Intravenous fluids is incorrect. IV fluids would be indicated if there was evidence of pancreatitis, or if the patient was hemodynamically unstable. In this case, the patient has severe anaemia, but in the context of haemodynamic stability IV fluids would be inappropriate as they would lead to a further drop in Hb concentration via a dilutional effect.

Liver transplantation is incorrect. The King's college criteria state that for non-paracetamolinduced liver injury an INR >6.5 or three from; bilirubin of greater than 600µmol/L, an interval of >7 days between jaundice and encephalopathy, age <10 years or >40, INR >3.5, drug-induced or indeterminate cause of hepatitis, would be poor prognostic features and indicate liver transplant may be required.

Oral prednisolone is incorrect. This would be an option for alcoholic hepatitis or autoimmune haemolytic anaemia. In this case, the direct coomb's test is negative indicating that the low haemoglobin is not a result of immune-mediated haemolysis.

Question 62 of 89

A 52-year-old male was seen in the rapid access Transient Ischaemic Attack (TIA) clinic. He presented to his GP with new onset left leg and arm weakness three days ago. The weakness lasted for 90 minutes and fully resolved with no residual defect. He had a past medical history of hypertension, obstructive sleep apnoea and a left sided deep vein thrombosis eight years ago. His medication comprised ramipril 5mg OD. He smoked ten cigarettes per day and did not drink alcohol.

On examination, he had obvious truncal obesity and a flushed complexion. Blood pressure was 128/82 mmHg, heart rate 78/min, respiratory rate 16/min and oxygen saturations 99% on air. Cardiovascular examination revealed a regular pulse and nil else of note. Respiratory and gastrointestinal examination were normal, though examination of the abdomen was somewhat limited by the presence of truncal obesity. Neurological examination was unremarkable with normal cranial nerve, fundoscopy and peripheral neurological examinations.

Initial investigations revealed the following results:

Hb	191 g/l
MCV	98 fl
Hct	0.523
Platelets	502 * 10 /l
WBC	14.0 * 10 /l
Neutrophils	86%
Lymphocytes	10%
Monocytes	4%
HbA1c	43 mmol/mol
Fasting cholesterol	5.6 mmol/l

ECG: 76bpm normal sinus rhythm no other abnormality Chest x-ray: unremarkable

24 hr ECG: no arrhythmia seen

Echo: normal systolic function, mild aortic stenosis with pressure gradient of 42mmHg

CT head: normal intracranial appearances, no evidence of mass shift, space occupying lesion or haemorrhage

What is the most appropriate next investigation most likely to lead to the underlying diagnosis?

A. Cardiac catheterization
B. Testing for presence of JAK2 mutation
C. Bone marrow biopsy
D. Radioisotope scanning of circulating blood volumes
E. MRI scanning of the abdomen

B. Testing for presence of JAK2 mutation

This gentleman has polycythaemia rubra vera (PRV). Whilst all of the above investigations may facilitate the diagnostic process, this question asks *What is the most appropriate next investigation most likely to lead to the underlying diagnosis?*. Testing for JAK2 mutation has widely surpassed the use of radioisotope scanning and is diagnostic of PRV. It is, therefore, the best option

. Question 63 of 89

An 18-year-old man presents to the emergency department with headache and discolouration of his face. He has a past medical history of NADH methaemoglobinaemia reductase deficiency. He does not smoke cigarettes or drink alcohol.

His observations are as follows: heart rate 94 beats per minute, oxygen saturations 85% on room air, blood pressure 120/77 mmHg, respiratory rate 20/minute and temperature 37ºC.

Despite administration of 15L of oxygen via a non-rebreathe mask, the Sp2 remains 85%. On examination, he appears cyanotic. The cardiorespiratory examination is unremarkable.

Plain radiography of the chest is normal.

ABG results:

pH	7.36	(7.35-7.45)
pO2	11 kPa	(11-13)
pCO2	4 kPa	(4-6)
Hb	136 g/L	(135-175)
Lactate	2.0 mmol/L	(0-2)
MetHb	30%	(0.2-0.6)

What is the most appropriate treatment?

A. Antibiotic treatment
B. Ascorbic acid
C. Methylene blue
D. No specific treatment
E. Thrombolysis

B. Ascorbic acid

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

Ascorbic acid is correct. This patient has NADH methaemoglobinaemia reductase deficiency, which is a congenital form of methaemoglobinaemia. IV methylene blue is ineffective in this form of the disease. He has evidence of a deterioration in his condition requiring treatment with a methaemoglobin level >= 30%, cyanosis, headache and a low peripheral oxygen saturation level despite normal arterial oxygen content. Ascorbic acid has been shown to be effective in the treatment of this disorder.

Methylene blue is incorrect. This is not effective in this form of methaemoglobinaemia but is the typical treatment for acquired causes.

Antibiotics treatment is incorrect. The patient is apyrexial with a normal chest x-ray and there no history of cough or shortness of breath. An infection seems unlikely.

No specific treatment is incorrect. Symptoms and a methaemoglobin level >= 30% are both indications for treatment in this condition.

Thrombolysis is incorrect. While a pulmonary embolism is a plausible cause of low peripheral oxygen saturations with a normal examination and chest x-ray, the clinical context otherwise does not suggest this as the diagnosis. Furthermore, the typical indication for thrombolysis in pulmonary embolism is hypotension, which is absent in this case.

Question 64 of 89

A 34 year old man is admitted under the medics from the emergency department with central abdominal pain and vomiting

not responding to IV morphine. He had been seen by the surgeons earlier in the day as an acute abdomen, but the CT scan they did of his abdomen and pelvis revealed no abnormalities, and his bloods suggested no surgical cause of the abdominal pain.

You note that the patient has presented to the emergency department five times in the past two years with similar problems, and no cause has ever been found, with the patient being discharged one or two days later with analgesia.

On examination his abdomen is generally tender with evidence of voluntary guarding. On further examination you note that he has a rash on the back of his hands, neck and cheeks. This rash consists of several small fluid filled bullae.

His past medical history includes depression - for which he is taking citalopram, and one short psychiatric inpatient stay for an episode of psychosis.

What is the most likely diagnosis?

A. Erythropoietic protoporphyria
B. Porphyria cutanea tarda
C. Hereditary coproporphyria
D. Acute intermittent porphyria
E. Congenital erythropoietic porphyria

D. Acute intermittent porphyria

The porphyrias are a group of rare inborn errors of metabolism caused by abnormalities of enzymes involved in the biosynthesis of haem, resulting in overproduction of intermediate compounds called porphyrins.

Three patterns of symptoms occur clinically with porphyrias:

1) Neurovisceral - neuropathy, epilepsy, psychiatric disorders, abdominal, vomiting, constipation

2) Photosensitive - bullous eruption in sun exposed areas

3) Haemolytic

Neurovisceral only	Photosensitive only	Mixed
Acute intermittent porphyria	Porphyria cutanea tarda	Variegate porphyria
Aminolaevulinic acid dehydrogenase porphyria	Congenital erythropoietic porphyria	Hereditary coproporphyria
-	Erythropoietic protoporphyria	-

This patient has both photosensitive symptoms; his rash, and neurovisceral symptoms; abdominal pain and previous psychiatric history. The only mixed presentation porphyria given as a possible answer is hereditary coproporhyria, hence it is the correct answer.

Question 65 of 89

A 62 year old man is attending his GP as part of regular screening. He has a past medical history significant only for hypertension for which he has been taking amlodipine for many years. He reports no specific symptoms of note and is still working full time as an accountant. His blood pressure on this visit is 132/78mmHg and his urinalysis shows no abnormalities. Blood tests were taken for routine monitoring.

Hb	13.8 g/dl
Platelets	362 * 10 /l9
WBC	6.3 * 10 /l9
Na +	142 mmol/l
K +	4.2 mmol/l
Urea	4.6 mmol/l
Creatinine	84 µmol/l
Adjusted calcium	2.41mmol/l
Lactate Dehydrogenase	300 IU/l
Albumin	36 g/l
Globulin	52 g/l

An abnormal protein band is detected during analysis and the GP arranges for further review with the Haematologist at the hospital. Further investigations are undertaken:

Monoclonal paraprotein 18g/l

Bone Marrow examination showing 6% plasma cells Skeletal Survey showing no abnormalities

What is the diagnosis?

A. Multiple Myeloma
B. Hodgkins Lymphoma
C. Waldenstrom's macroglobulinemia (lymphoplasmacytic lymphoma)
D. Asymptomatic Myleoma
E. Monoclonal gammopathy on uncertain significance (MGUS)

E. Monoclonal gammopathy on uncertain significance (MGUS)

Monoclonal gammopathy on uncertain significance (MGUS) is a condition where an abnormal paraprotein is found in the blood, often during routine testing. It is on a spectrum that includes multiple myeloma but at the MGUS stage no treatment is indicated. The level of serum paraprotein is lower than in myeloma (under 30g/l) and the number of plasma cells in the bone marrow is also lower (less than 10%). The condition is totally asymptomatic. There is an annual risk of progression to myeloma of 1-2% and as such annual surveillance is recommended.

The diagnosis of MGUS can be made in patients who fulfil the following criteria –

- A monoclonal paraprotein band lesser than 30 g/L (< 3g/dL)
- Plasma cells less than 10% on bone marrow examination
- No evidence of bone lesions,anemia, hypercalcemia, or renal insufficiency related to the paraprotein
- No evidence of another B-cell proliferative disorder

In terms of myeloma this can be classified as below, taking note of both asymptomatic and symptomatic myeloma:

Symptomatic myeloma:

- Clonal plasma cells >10% on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (plasmacytoma)
- A monoclonal protein (paraprotein) in either serum or urine (except in cases of true nonsecretory myeloma)
- Evidence of end-organ damage felt related to the plasma cell disorder (related organ or tissue impairment, ROTI, commonly referred to by the acronym 'CRAB'):
- hyperCalcemia (corrected calcium >2.75mmol/L)
- Renal insufficiency attributable to myeloma
- Anemia (hemoglobin <10 g/dL)

- Bone lesions (lytic lesions or osteoporosis with compression fractures)

Asymptomatic (smoldering) myeloma:

- Serum paraprotein >30 g/L AND/OR
- Clonal plasma cells >10% on bone marrow biopsy AND
- NO myeloma-related organ or tissue impairment

Question 66 of 89

You are the medical doctor on an acute admission unit. An elderly female with recently diagnosed ovarian cancer, who is on day 8 of cisplatin chemotherapy presents with a temperature of 39°C, tachycardia at 130 bpm, blood pressure 128/68 mmHg, respiratory rate 14/min, sats 98% on room air.

She is complaining of abdominal pain and has been vomiting today. Her bloods and blood culture have been sent and you are awaiting the results. Her chest x-ray was normal and urine dipstick clear.

What is the most appropriate antibiotic therapy to start her on?

A. IV benzylpenicillin + flucloxacillin
B. IV augmentin
C. IV ciprofloxacin
D. IV piperacillin/tazobactam
E. IV piperacillin/tazobactam + gentamicin

D. IV piperacillin/tazobactam

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

The patient has presented with a systemic inflammatory response syndrome (SIRS) - tachycardia, pyrexia. The most likely cause for this would be an infection and she should be treated as a probable neutropenic sepsis until proven otherwise. Neutropenic sepsis tend to present on day 7- 10 post-chemotherapy. Given that we are unable to determine the source of infection, she should ideally be treated with a broad-spectrum antibiotic such as IV piperacillin/tazobactam. You would also normally add a stat dose of gentamicin but given that she was on cisplatin therapy, the combination of these 2 medications would be highly nephrotoxic and should be witheld until neutropenic sepsis is confirmed and renal function results are available.

Question 67 of 89

An 82-year-old man presents with a 6-month history of 8 kg of weight loss, fevers, and night sweats. On examination, he has cervical and inguinal lymphadenopathy and a mildly enlarged spleen. Blood results are as follows:

Hb	101 g/L	Male: (135-180)Female: (115 - 160)
Platelets	142 * 10 /L 9	(150 - 400)
WBC	40.5 * 10 /L 9	(4.0 - 11.0)
Neuts	2.8 * 10 /L 9	(2.0 - 7.0)
Lymphs	34 * 10 /L 9	(1.0 - 3.5)

Given the most likely diagnosis, what would be the diagnostic investigation of choice?

A. Bone marrow aspirate / trephine
B. CT neck, chest, abdomen and pelvis
C. Flow cytometry (immunophenotyping)
D. HIV test
E. Lymph node biopsy

C. Flow cytometry (immunophenotyping)

CLL - immunophenotyping is investigation of choice

The diagnosis is most certainly CLL which is the most common cause of significant lymphocytosis in an elderly patient.

CLL has a very specific immunophenotype and can thus be diagnosed on **flow cytometry** of peripheral blood.

Although a **bone marrow examination** and **lymph node biopsy** would also likely be diagnostic of CLL, they are invasive tests and thus should only be performed if immunophenotyping was nondiagnostic. A **CT neck, chest, abdomen, and pelvis** would be useful for staging, however, it would not be particularly helpful in making the diagnosis.

HIV can cause an early mild lymphocytosis (due to a CD8 lymphocytosis) however it is most often associated with lymphopaenia. The patient's age and presence of a marked lymphocytosis favour the diagnosis of CLL.

Question 68 of 89

A 39-year-old woman presents with anaemia secondary to menorrhagia. She has a past medical history of fibroids, rhesus incompatibility in pregnancy 9 years ago, and Hodgkin's lymphoma which has been in remission for 21 years.

She has a severe penicillin allergy. Her investigations show the following:

Hb	59 g/L	Female: (115 - 160)
Platelets	350 * 10 /L 9	(150 - 400)
WBC	4.7 * 10 /L 9	(4.0 - 11.0)

Pregnancy test: negative.

The consultant asks for you to prescribe her 2 units of packed red cells.

What requirement would apply to this patient's blood transfusion?

A. Give antihistamines with packed red cells
B. No special requirements
C. Use CMV negative packed red cells
D. Use irradiated packed red cells
E. Use washed red blood cells

D. Use irradiated packed red cells

Hodgkin lymphoma is an indication for irradiated blood products

The patient would require **irradiated** packed red cells due to her history of Hodgkin's lymphoma. Irradiated blood is treated with radiation which prevents lymphocyte division which can cause transfusion-associated graft-versus-host disease (TA-GvHD). A history of Hodgkin's lymphoma increases the risk of this reaction

and hence all red cell, platelet, and granulocyte concentrates should be irradiated for life.

No special requirements is incorrect because this patient requires irradiated blood as explained above.

There is no indication for **antihistamines** to be given with packed red cells for this patient. Like all patients, she should be monitored for any signs of allergic reaction regularly during her transfusion but only treated for this if this occurs.

CMV negative blood is blood collected from donors who have tested negative for CMV IgG antibodies. CMV can cause serious infections in immunocompromised patients and is the most common cause of congenital infection cause developmental abnormalities in the UK. CMV negative blood should be used for intrauterine transfusions, neonates up to 28 days post expected delivery and for transfusions during pregnancy. There is no indication for CMV negative blood in this patient.

Washed red cells are used when there are recurrent and/or severe allergic reactions to transfusion and can also be used for IgA deficient patients with anti-IgA antibodies. This patient has a penicillin allergy but not to blood products.

Question 69 of 89

A 47-year-old woman with a background of obesity is admitted with left leg cellulitis. Blood cultures are taken and she is commenced on IV flucloxacillin.

Shortly afterwards, you are asked to see her as she has become itchy and light-headed in the last 5 minutes. Observations are as follows.

Respiratory rate 30 breaths per minute Oxygen saturations 90% on air Heart rate 127 beats per minute Blood pressure 75/42mmHg Temperature 36.8°C

Chest examination reveals widespread wheeze. The rest of the examination is unremarkable, other than her cellulitis which has not spread beyond the markings.

What statement is correct concerning the suspected diagnosis?

A. An elevated tryptase that remains at the same level after 2 hours supports the diagnosis
B. High tryptase now confirms the diagnosis
C. Normal tryptase at 24 hours excludes the diagnosis
D. Normal tryptase now excludes the diagnosis
E. Normal tryptase now that becomes elevated in 2 hours supports the diagnosis

A. Normal tryptase now that becomes elevated in 2 hours supports the diagnosis

Anaphylaxis - serum tryptase levels rise following an acute episode

The correct answer is **normal tryptase now that becomes elevated in 2 hours supports the diagnosis**. The features of cardiovascular collapse, breathing difficulty and bronchospasm following IV antibiotics are suggestive of anaphylaxis. Tryptase is released into the blood in the context of mast cell degranulation. In anaphylaxis, it is expected to rise quickly in the first minutes to hours before gradually falling. NICE recommend it is measured at baseline and after 1-2 hours (but no later than 4). If measured at onset, it may be normal - the key finding is the elevation over the first few hours. If measured after 4 hours, it may have returned to normal.

An elevated tryptase that remains at the same level after 2 hours supports the diagnosis is incorrect. Some patients have elevated tryptase at baseline, for example in the context of systemic mastocytosis. It can also cross-react, for example with rheumatoid factors, leading to elevated levels in the absence of anaphylaxis. The lack of a change over 2 hours is more suggestive of a high baseline rather than anaphylaxis, where we would expect a significant change from onset to 2 hours.

High tryptase now confirms the diagnosis is incorrect. A single elevated measurement does not confirm the diagnosis for the reasons described above - a second sample must be taken within the next few hours to check for a change from baseline.

Normal tryptase at 24 hours excludes the diagnosis is incorrect. By 24 hours, we would expect the tryptase level to have returned to baseline, even in a significant anaphylactic episode. A baseline level and a 1-2 hour level would be much more helpful.

Normal tryptase now excludes the diagnosis. Tryptase level at the onset of symptoms may be normal as it takes at least 15 minutes (but longer in some patients) to mount a response, and we are told the symptoms have lasted 5 minutes here. A single measurement has limited utility, and we would have to repeat the sample at 1-2 hours for more useful information.

Question 70 of 89

A 17-year-old man presents to the acute medical unit with shortness of breath. He takes no regular medicines and denies the use of any recreational, herbal, or over-the-counter medications. He has not been exposed to any local anaesthetics or chemicals. On examination, his chest was clear on auscultation and he was markedly cyanotic. Despite the cyanosis, his SpO2 is 92%.

You start the patient on 15L O2 via a non-rebreather mask. Blood gas analysis results are as follows:

pH	7.28	(7.35 - 7.45)
PaO2	66.5 kPa	(10.3 - 13.3 kPa)
PaCO2	2.8 kPa	(4.7 - 6 kPa)
HCO3	22 mmol/L	(22 - 28 mmol/L)
SaO2	52%	(94-98)

The patient moved to the UK from India 6 weeks ago. His medical records are not available. However, he advises you that he has a 'blood disorder' that runs in his family.

Given the most likely diagnosis, what is the treatment of choice?

A. 4-Dimethylaminophenol
B. Ascorbic acid
C. C1-inhibitor concentrate
D. Hydroxocobalamin
E. Hyperbaric oxygen

B. Ascorbic acid

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase Deficiency

The striking feature, in this case, is the significant discrepancy between the PaO2 and SaO2. Given the patient is on 15L O2, the PaO2 is at a level expected indicating that gas exchange at the level of the alveoli is not impaired. However, the SaO2 is markedly low at 52% indicating impaired oxygen binding to haemoglobin. The main two causes of this picture are methaemoglobinaemia and carboxyhemoglobinemia. The family history is indicative of familial NADH methaemoglobinaemia reductase deficiency.

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency.

Hyperbaric oxygen is the treatment of choice for severe carbon monoxide poisoning. Although carbon monoxide poisoning presents similarly and remains within the differential diagnosis, the positive family history makes congenital methaemoglobinaemia the more likely diagnosis.

4-Dimethylaminophenol and **hydroxocobalamin** can be used for the treatment of cyanide poisoning. Cyanide binds the ferric (Fe3+) ion of cytochrome oxidase causing 'histotoxic hypoxia' and lactic acidosis. It would not cause a marked reduction of SaO2 as seen in this case unless it was associated with coexistent carbon monoxide poisoning (e.g. due to smoke inhalation). There is nothing in this case to suggest that this is the case.

C1-inhibitor concentrate remains the gold standard treatment for the acute management of hereditary angioedema. The clinical and laboratory features, in this case, are not in keeping with hereditary angioedema which presents with recurrent attacks of self-limiting oedema affecting the skin, gastrointestinal tract, and airways.

Question 71 of 89

A 36-year-old man is brought to the emergency department following a motor vehicle accident. He is drowsy but conscious. He has an open fracture on the right anterior shin which is bleeding profusely. Vital sign monitoring reveals that he has a respiratory rate of 22 bpm, heart rate of 118 bpm, blood pressure of 92/55 mmHg and temperature of 37.1 degrees Celsius. In an attempt to resuscitate the patient, the doctor decides to transfuse 2 pints of group O negative blood. A few minutes after giving the blood, the nurse notices that the patients developed a generalized rash and swelling of the lips, associated with a loud breathing sound. His medical notes reveal that he has atopy and has been treated for giardiasis multiple times previously.

Which one of the following conditions could possibly represent a predisposition to the patient's condition?

A. Von Willebrand disease
B. Hairy cell leukemia
C. Selective IgA deficiency
D. Severe combined immunodeficiency
E. Wiskott-Aldrich syndrome

C. Selective IgA deficiency

IgA deficiency is associated with anaphylactic reaction to blood products

This patient presented after a motor vehicle accident with an open fracture wound. The vital signs pointed towards a hypovolemic shock secondary to blood loss from the fracture wound and also possibly secondary to an internal injury, such as a spleen laceration. The patient was transfused with group O negative blood, which is the universal donor blood group, but developed an anaphylactic reaction. This is quite unusual given that the blood was group O negative. Anaphylactic reactions to products are common among individuals with selective IgA deficiency. Selective IgA deficiency is the most common primary immunodeficiency and individuals with this condition have low IgA levels despite normal levels of the IgG and IgM. Patients often suffer from recurrent airway infections, atopy, autoimmune diseases and are prone to have giardiasis infection. To avoid this, these patients must receive blood products without IgA.

1: Von Willebrand disease is a coagulation disorder which affects intrinsic pathway and is due to deficient von Willebrand factor. This leads to an impairment in the formation of the platelet plug. There is no increased risk of anaphylaxis to blood products in patients with this condition.

2: Hairy cell leukemia is one type of lymphoid neoplasm with the cells having hair-like projections and hence the name of the condition. The disease leads to bone marrow fibrosis. There is no increased risk of anaphylaxis to blood products in patients with this condition.

4: Severe combined immunodeficiency is a type of immunodeficiency which involves both a B and T-cell disorder. There are different types comprising IL-2R gamma chain deficiency and adenosine deaminase deficiency. Patients often present with failure to thrive, thrush and diarrhea. They have an increased susceptibility to infections from several types of microorganisms such as viruses, fungi, protozoan, and bacteria. There is no increased risk of anaphylaxis to blood products in patients with this condition.

5: Wiskott-Aldrich syndrome is a type of immunodeficiency which involves both a B and T-cell disorder. It is due to a mutation on the WASp gene causing platelets and leukocytes to be unable to carry out antigen presentation due to a defective actin cytoskeletal reorganization. Patients often present with the triad of thrombocytopenia, recurrent pyogenic infections, and eczema. There is no increased risk of anaphylaxis to blood products in patients with this condition.

Question 72 of 89

A 35-year-old patient presents to a rural emergency department with abdominal pain and facial swelling. He has a past medical history of C1 esterase inhibitor deficiency. He has recently arrived from Belarus and does not have any of his regular medications. He does not smoke cigarettes or drink alcohol.

His observations are heart rate 88 beats per minute, blood pressure 122/78mmHg, respiratory rate 18/minute, oxygen saturations 96% on room air and temperature 37ºC.

On examination, there is facial swelling without airway compromise. There is mild abdominal tenderness without any evidence of peritonism. There is no rash or wheeze.

Unfortunately, there is no possibility of locating IV C1-inhibitor concentrate in this rural setting. Given the clinical history,

what is the most appropriate medication to abort the attack?

A. Adrenaline
B. Danazol
C. Fexofenadine
D. Fresh frozen plasma
E. Prednisolone

D. Fresh frozen plasma

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

Fresh frozen plasma is the correct answer. This is an available option for treating acute attacks of hereditary angioedema (HAE) if IV C1-inhibitor concentrate is not available.

Danazol is incorrect. This is a gonadotropin inhibitor used in the prophylaxis of HAE rather than in the management of acute attacks.

Fexofenadine, prednisolone and adrenaline are all incorrect. They are ineffective in managing the swelling associated with this condition. The postulated theory is that histamine-mediated angioedema responds to these interventions but bradykinin mediated angioedema is resistant. Bradykinin is the principal mediator of symptoms in HAE.

Question 73 of 89

A 73-year-old woman is reviewed routinely in haematology clinic. She has a diagnosis of chronic lymphocytic leukaemia. She is not on any treatment but remains under regular review. She has lost 5% of her body weight in the last 9 months. She reports occasional fatigue. She does not smoke cigarettes or drink alcohol. She lives alone and is independent.

On examination, there are two 0.5cm lymph nodes palpable in her neck, which were palpable at her previous appointment.

Blood tests at the time of clinic review:

Hb	122 g/L	Male: (135-180)Female: (115 - 160)
Platelets	75 * 10 /L 9	(150 - 400)
WBC	14 * 10 /L 9	(4.0 - 11.0)
Neuts	6.0 * 10 /L 9	(2.0 - 7.0)
Lymphs	7.8 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.0 * 10 /L 9	(0.0 - 0.4)

Blood tests two months ago:

Hb	123 g/L	Male: (135-180)Female: (115 - 160)
Platelets	189 * 10 /L 9	(150 - 400)
WBC	13.5 * 10 /L 9	(4.0 - 11.0)
Neuts	6 * 10 /L 9	(2.0 - 7.0)
Lymphs	7.3 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.0 * 10 /L 9	(0.0 - 0.4)

What patient-specific factor does this patient possess that warrants commencing treatment for her underlying malignancy?

A. Fatigue
B. Weight loss
C. Lymphadenopathy
D. Progressive lymphocytosis
E. Thrombocytopenia

A. Thrombocytopenia

Thrombocytopenia -> indication to start treatment in CLL

Thrombocytopenia is the correct answer. The development of thrombocytopenia is an indication to start treatment in CLL.

Fatigue is incorrect. While extreme fatigue may be an indication to start treatment, this patient reports only occasional fatigue and therefore treatment is not warranted on this basis.

Progressive lymphocytosis is incorrect. This patient has a < 50% increase in lymphocyte count over the course of two months and therefore does not meet criteria to start treatment on this basis.

Lymphadenopathy is incorrect. The lymphadenopathy needs to be either massive (>10cm) or progressive to warrant treatment and it is neither.

Weight loss is incorrect. This patient has lost 5% of her body weight in 9 months. She would need to have lost 10% in approximately six months to warrant treatment.

Question 74 of 89

A 67-year-old male with known chronic lymphocytic leukaemia (CLL) currently under monitoring only presents to his general practitioner. He has developed new fevers and reports his pillow being wet. He has a dry cough and has lost a few pounds in weight but otherwise feels well. He is otherwise well and has hypertension and type 2 diabetes. He was taking amlodipine, metformin and tolbutamide but has stopped these two weeks prior due to his prescription not being renewed. He is a smoker and drinks alcohol 10-14 units a week.

On examination, his temperature is 37.9ºC and his chest is clear. He is clammy but there are no visible rashes.

Hb	124 g/l
Platelets	378 * 10 /l9
WBC	13.2 * 10 /l9
Neuts	11.2* 10 /l9
CRP	9mg/L
LDH	857 U/L (normal range 180-360 U/L)

What is the likely explanation?

A. Drug withdrawal reaction
B. Richter's transformation
C. Lower respiratory tract infection (LRTI)
D. Glandular fever
E. Neutropaenic sepsis

B. Richter's transformation

New B-symptoms in CLL -> Richter's transformation

This gentleman presents with new fevers and night sweats on a background of CLL which is normally controlled. He notably has a raised lactate dehydrogenase (LDH) and these symptoms in the context of haematology are B-symptoms. He is not neutropenic. Glandular fever would not explain the night sweats and fevers and usually presents with fatigue and a sore throat. The medications would not cause isolated fever as a withdrawal reaction. A LRTI is possible but there is only a dry cough and no chest signs. We know that 5% of CLL will undergo Richter's transformation becoming a high grade lymphoma with new B-symptoms and crucially a rise in LDH which makes this the likeliest answer.

Question 75 of 89

A 53-year-old man presents with abdominal pain. He was seen six weeks ago by surgeons who diagnosed gastritis and offered omeprazole. He initially improved but the pain recurred and he has no benefit with omeprazole or gaviscon. He feels full quickly but has no dysphagia or regurgitation. He denies any heartburn. He reports general low energy and is sleeping more hours in the day and can fall asleep at any time.

On examination, a mass is palpable in the epigastrium. It has a palpable indent and you cannot get above it. There are bowel sounds and no other masses are felt. There are some isolated left axillary lymph nodes palpable. His temperature is 37.8ºC and heart rate is 78 beats per minute.

Hb	114 g/l
Platelets	289 * 10 /l9
WBC	51 * 10 /l9

What is the likeliest underlying diagnosis?

A. Gastric carcinoma
B. Visceral leishmaniasis
C. Chronic myelogenous leukaemia (CML)
D. Obstructive sleep apnoea (OSA)
E. Narcolepsy

C. Chronic myelogenous leukaemia (CML

CML may present with massive splenomegaly

This gentleman presents with abdominal pain and a new mass that based on location is likely spleen, stomach or left kidney. OSA and narcolepsy explain the sleepiness but not the abdominal symptoms. Gastric carcinoma with outlet obstruction can give a mass but usually there is vomiting or regurgitation of food contents. The mass is therefore likely to be spleen of which CML and leishmaniasis are the commonest causes. Leishmaniasis is less common making CML the likeliest diagnosis. Furthermore, the WBC is through the roof supporting CML as the cause.

Question 76 of 89

A 12-year-old boy is referred by his paediatrician to a tertiary immunology service. Since infancy, he has suffered from recurrent infections. He has required multiple courses of antibiotics for episodes of sinusitis, otitis media and pneumonia. Heel prick testing was normal perinatally. The referral was ultimately made after he had a prolonged admission to the paediatric intensive care unit with respiratory failure requiring intubation, where he was diagnosed with *Pneumocystis jirovecii* pneumonia. HIV testing was negative. In addition to recurrent infections, he has had chronic diarrhoea, for which no cause has been found. He is on no regular medications. He does not smoke or drink alcohol and is doing well in school despite his frequent illnesses. His parents attend the appointment with him.

Clinical examination revealed a thin adolescent. There was evidence of stomatitis and gingivitis. There was no organomegaly or lymphadenopathy. The cardiovascular and respiratory examination was unremarkable. There were no rashes. Neurological examination is unremarkable.

Blood tests:

Hb	124 g/L	Male: (135-180)Female: (115 - 160)
Platelets	144 * 10 /L	(150 - 400)
WBC	3.2 * 10 /L	(4.0 - 11.0)
Neuts	1.5 * 10 /L	(2.0 - 7.0)
Lymphs	0.8 * 10 /L	(1.0 - 3.5)
Mono	0.6 * 10 /L	(0.2 - 0.8)
Eosin	0.3 * 10 /L	(0.0 - 0.4)
Na	136 mmol/L	(135 - 145)
K	4.4 mmol/L	(3.5 - 5.0)
Urea	5.2 mmol/L	(2.0 - 7.0)
Creatinine	77 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Bilirubin	8 µmol/L	(3 - 17)
ALP	77 u/L	(30 - 100)
ALT	16 u/L	(3 - 40)
Î³GT	44 u/L	(8 - 60)
Albumin	32 g/L	(35 - 50)
Immunoglobulin A	0.4 g/L	(0.6-5.0)
Immunoglobulin M	2.6 g/L	(0.53 - 2.47)
Immunoglobulin G	5.4 g/L	(6.60 - 15.90)

What is the likely diagnosis?

A. Coeliac disease
B. Cystic fibrosis
C. Hyper IgM syndrome
D. Malnutrition
E. X-linked congenital agammaglobulinaemia

C. Hyper IgM syndrome

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis* pneumonia, hepatitis, diarrhoea

Hyper IgM syndrome is correct. This is usually x-linked and therefore affects males. It is characterized by recurrent bacterial infections, chronic diarrhoea and infection with atypical organisms such as Pneumocystis. It may also be associated with autoimmune anaemia, neutropenia and thrombocytopenia. Patients often have stomatitis and gingivitis. IgM may either be normal or high. IgG and IgA will be low as the condition causes an inability to class switch from IgM.

Bruton's (x-linked) congenital agammaglobulinaemia is incorrect. This causes recurrent bacterial infections but all immunoglobulin subclasses will be low including IgM.

Cystic fibrosis is incorrect. While it would cause recurrent chest infections, heel prick testing as a newborn being normal makes this diagnosis unlikely.

Coeliac disease is incorrect. This can cause a thin habitus and diarrhoea but would not explain the other findings.

Malnutrition is incorrect. While this can predispose to infection, there is no reason to believe he is not being cared for properly. We are told he is doing well in school and has supportive parents that attend his hospital appointments.

Question 77 of 89

A 74-year-old man is seen in the haematology clinic. He was diagnosed with chronic lymphocytic leukaemia 6 months ago following an incidental finding of lymphocytosis on some routine blood tests with his General Practitioner. He is currently under surveillance monitoring.

Over the last 6 months he has generally been in good health. He has occasional fatigue particularly towards the end of the day but remains to have a good appetite and reports no change in his weight. Only for the last week has he reported to be feeling more unwell with intermittent fevers and chills.

On examination he is febrile at 38.3ºC. He is mildly tachycardic with a heart rate of 114bpm and a blood pressure of 133/79mmHg. His chest is clear and heart sounds are normal. His abdomen is soft and non-tender. There is palpable 2cm splenomegaly.

Full blood count (6 months ago):

Hb	148 g/L	Male: (135-180)Female: (115 - 160)
WBC	49.3 * 10 /L 9	(4.0 - 11.0)
Lymphocytes	46.3 * 10	(0.8 - 5.0)
Neutrophils	2.7 * 10	(2.5 - 7.5)
Platelets	200 * 10 /L 9	(150 - 400)

Full blood count (today):

Hb	127 g/L	Male: (135-180)Female: (115 - 160)
WBC	75.6 * 10 /L 9	(4.0 - 11.0)
Lymphocytes	69.4 * 10	(0.8 - 5.0)
Neutrophils	3.8 * 10	(2.5 - 7.5)
Platelets	102 * 10 /L 9	(150 - 400)

Blood film: smudge cells seen.

Which of the following is an indication to start treatment in this patient?

A. Splenomegaly
B. Presence of fever for 1 week
C. White cell count > 75
D. Presence of smudge cells on peripheral blood film
E. Thrombocytopenia

A. Thrombocytopenia

Thrombocytopenia -> indication to start treatment in CLL

This patient has a new thrombocytopenia compared to his blood tests 6 months ago. A new thrombocytopenia or sign of bone marrow failure is an indication to initiate treatment. Treatment options vary depending on the patient's overall health, co-morbidities and prognostic factors.

Massive splenomegaly > 5cm is an indicator to start treatment. However, this patient has a 2cm splenomegaly which does not make it an indicator for starting treatment.

Recurrent infections or fevers persisting beyond 2 weeks are indicators for starting treatment. This patient has had fevers for 1 week. However, if this continued then that would be a second indicator for starting treatment.

A rising lymphocyte count is an indicator for starting treatment. However, a doubling of lymphocytes in 6 months is needed which is not seen here.

Smudge cells are not an indicator for starting treatment.

Other indicators for starting treatment include: massive lymphadenopathy, constitutional symptoms including fever, weight loss or night sweats and the presence of haemolysis

Question 78 of 89

A 45-year-old man is referred to the haematology clinic with a 4-month history of easy bruising and prolonged bleeding. He denies any other symptoms and is otherwise feeling well. His past medical history includes rheumatoid arthritis that he reports is not well-controlled, with frequent flares. There is no family history of bleeding disorders.

Laboratory blood tests:

Hb	126 g/L	(135-180)
Platelets	201 * 10 /L 9	(150 - 400)
WBC	5.5 * 10 /L 9	(4.0 - 11.0)
Prothrombin time (PT)	12 secs	(10-14 secs)
Activated partial thromboplastin time (APTT)	45 secs	(25-35 secs)
Fibrinogen	2.2 g/L	(2 - 4)
D-Dimer	300 ng/mL	(< 400)
Von Willebrand Factor	100 IU/dL	(50-150)
Factor VIII levels	Reduced	

What is the most likely diagnosis?

A. Acquired haemophilia A
B. Beta thalassaemia trait
C. Christmas disease
D. Factor V Leiden
E. Von Willebrand's disease

A. Acquired haemophilia A

Acquired haemophilia A is diagnosed in patients without previous or familial histories of bleeding who have isolated prolongation of the activated partial thromboplastin time (aPTT), reduced FVIII levels as well as evidence of FVIII inhibitor activity

This patient has a diagnosis of acquired haemophilia A, an autoimmune disorder secondary to antibody production against factor VIII. Unlike congenital haemophilia A, acquired haemophilia A develops later in life. Up to 50% of cases of acquired haemophilia A are associated with co-existing

autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus and inflammatory bowel disease. The investigation findings are similar to congenital haemophilia A and include a raised aPTT and reduced FVIII levels. The presence of antibodies to factor VIII helps to differentiate between congenital and acquired causes.

Beta thalassaemia trait is a disorder of haemoglobin chain production, causing microcytic anaemia. Symptoms include those associated with anaemia such as pallor, shortness of breath and fatigue. Bruising and bleeding are not common features and beta thalassaemia trait does not explain this patient's clotting abnormalities.

Christmas disease (also known as haemophilia B) is an inherited coagulation disorder associated with reduced levels of factor IX. It has no impact on factor VIII levels and cannot explain this patient's laboratory findings.

Factor V Leiden (also known as activated protein C resistance) is the most common cause of thrombophilia. Rather than increasing bleeding, increased coagulation is seen, including an increased risk of deep vein thromboses. Therefore, factor V Leiden is incorrect.

Von Willebrand's disease is the most common inherited bleeding disorder. Symptoms include epistaxis, menorrhagia and gum bleeding. Similarly to this patient, coagulation studies demonstrate a prolonged APTT and reduced factor VIII levels. However, the presence of factor VIII inhibitor activity makes a diagnosis of Von Willebrand's disease less likely and points toward an autoimmune cause of this patient's symptoms.

Question 79 of 89

A 65-year-old female, known to have metastatic breast carcinoma presents to the hospital with a 24-hour history of increasing pain, swelling and erythema of her right calf. She is otherwise relatively well. She was diagnosed with breast carcinoma four years previously and was initially treated with surgery, radiotherapy and chemotherapy. She was found to have disease recurrence with distant metastasis 12 months previously. She is known to have liver and bone metastases.

On examination, she appears pale and has some hair loss following recent chemotherapy. Apart from her swollen, erythematous, tender right calf and a fentanyl patch examination is unremarkable.

Bloods on admission show:

Hb	100 g/l
Platelets	180 * 10 /l9
WBC	7.2* 10 /l9
D-Dimer	1276 µg/L (normal <500µg/L)
Na +	132 mmol/l
K +	4.5 mmol/l
Urea	7.2mmol/l
Creatinine	110 µmol/l

She is diagnosed with a right leg deep vein thrombosis.

Given her current clinical condition, what is the best method of anticoagulation?

A. Low molecular weight heparin (LMWH) and warfarin until warfarin therapeutic followed bywarfarin therapy for 6 months then reassess.
B. Low molecular weight heparin (LMWH) for 3-6 months then reassess
C. Warfarin therapy starting with a slow loading regime for 6 months then reassess
D. Direct oral anticoagulants (DOACs) for 3-6 months then reassess
E. Referral for inferior vena cava filter insertion

D. Direct oral anticoagulants (DOACs) for 3-6 months then reassess

Cancer patients with VTE - 6 months of a DOAC

Question 80 of 89

A 68-year-old woman is reviewed in haematology clinic routinely. She has a past medical history of chronic lymphocytic leukaemia (CLL), characterised by a deletion of the short arm of chromosome 17 (17p).

On examination, there is cervical lymphadenopathy and splenomegaly. Blood tests:

Hb	115 g/L	Male: (135-180)Female: (115 - 160)
Platelets	189 * 10 /L 9	(150 - 400)
WBC	35.3 * 10 /L 9	(4.0 - 11.0)
Neuts	2.1 * 10 /L 9	(2.0 - 7.0)
Lymphs	33.0 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.0 * 10 /L 9	(0.0 - 0.4)
Na +	138 mmol/L	(135 - 145)
K +	4.2 mmol/L	(3.5 - 5.0)
Urea	5.1 mmol/L	(2.0 - 7.0)
Creatinine	88 µmol/L	(55 - 120)
CRP	4 mg/L	(< 5)
Lactate dehydrogenase (LDH)	180 U/L	(140-280)

Given the clinical history and underlying diagnosis, which clinical feature is associated with the worst prognosis?

A. Female sex
B. Age > 60
C. Lymphocyte count > 30
D. Normal LDH
E. 17p deletion

A. 17p deletion

del 17p is associated with a poor prognosis in CLL

17p deletion is the correct answer. The patient has chronic lymphocytic leukaemia. This a type of cancer in which the bone marrow makes too many lymphocytes, as evidenced in this case. The cancer in this case is characterized by a genetic mutation causing deletion of 17p, which is a part of chromosome 17. This is associated with a poor prognosis in CLL. It is seen in 5-10% of patients. The absence of part of chromosome 17 results in absence of one allele of the TP53 tumour suppressor gene, predisposing to the development of CLL.

Age > 60 is incorrect. Poor prognosis is associated with those > 70 years of age.Lymphocyte count > 30 is incorrect. Poor prognosis is

associated with those patients with lymphocyte counts > 50.Normal LDH is incorrect. A raised LDH implies a worse prognosis.Female sex is incorrect. Male sex implies a worse prognosis.

Question 81 of 89

A 24-year-old woman is admitted with a 1-hour history of worsening dyspnoea. On examination, you note stridor and marked angioedema of the lips and tongue. No rash is present. You immediately seek the assistance of the anaesthetic team to help secure the airway.

The patient has a history of hereditary angioedema. You are told that due to manufacturing issues, IV C1-inhibitor concentrate is not available.

What alternative treatment should be offered?

A. Danazol
B. Fresh frozen plasma
C. Intramuscular adrenaline
D. Intravenous methylprednisolone
E. Tranexamic acid

B. Fresh frozen plasma

Hereditary angioedema: the acute management is IV C1-inhibitor concentrate or fresh frozen plasma if this is not available

The correct answer is **fresh frozen plasma**. This is considered a second-line therapy where C1 inhibitor concentrate is not available as the plasma itself contains C1 inhibitor. No randomised control trials exist but a majority of case reports describe efficacy with signs of improvement described between 30 minutes and 12 hours.

Danazol is incorrect. This is a synthetic androgen that is used in prophylaxis of acute episodes in patients with hereditary angioedema. It has not been shown to provide any benefit in acute attacks.

Intramuscular adrenaline is incorrect. Similar to glucocorticoids, adrenaline is not effective in hereditary angioedema. Episodes of angioedema not responding to adrenaline may be one of the first clues to the diagnosis.

Intravenous methylprednisolone is incorrect. While glucocorticoids are used in histamine-driven angioedema, they are not effective in hereditary angioedema as the pathogenesis is driven by bradykinin rather than histamine. **Tranexamic acid** is incorrect. It has been used for prophylaxis but a minimal effect is seen when used for the treatment of acute attacks.

Question 82 of 89

A 35-year-old woman presents to the emergency department with a one day history of a fever. She has a past medical history of metastatic breast cancer and has received her most recent round of chemotherapy 8 days ago. She is not on any other regular medications.

Her observations are heart rate 111 beats per minute, blood pressure 96/58 mmHg, respiratory rate 22/minute, oxygen saturations 97% on room air and temperature 38.7ºC.

On examination, she is warm to touch with capillary refill time < 2 seconds. A bounding pulse is noted. There is no obvious localizing source of infection from the rest of the examination.

Urinalysis is unremarkable.

Plain radiography of the chest is normal. Blood tests:

Hb	121 g/L	Male: (135-180)Female: (115 - 160)
Platelets	389 * 10 /L 9	(150 - 400)
WBC	1.7 * 10 /L 9	(4.0 - 11.0)
Neuts	0.4 * 10 /L 9	(2.0 - 7.0)
Lymphs	0.9 * 10 /L 9	(1.0 - 3.5)
Mono	0.2 * 10 /L 9	(0.2 - 0.8)
Eosin	0.2 * 10 /L 9	(0.0 - 0.4)
Na +	137 mmol/L	(135 - 145)
K +	4.4 mmol/L	(3.5 - 5.0)
Bicarbonate	20 mmol/L	(22 - 29)
Urea	8.9 mmol/L	(2.0 - 7.0)
Creatinine	111 µmol/L	(55 - 120)
CRP	180mg/l	(<4)

What is the appropriate antibiotic choice?

A. Meropenem
B. Piperacillin/tazobactam
C. Piperacillin/tazobactam and gentamicin
D. Piperacillin/tazobactam and gentamicin and vancomycin
E. Piperacillin/tazobactam and vancomycin

B. Piperacillin/tazobactam

Piperacillin with tazobactam (Tazocin) is the empirical antibiotic of choice for neutropenic sepsis

Piperacillin/tazobactam is the correct answer. This patient has neutropenic sepsis secondary to chemotherapy treatment. This choice is supported by NICE guidelines and is first-line for the treatment of neutropenic sepsis.

Meropenem is incorrect. If the patient fails to respond after 48 hours then they may be escalated to meropenem.

Piperacillin/tazobactam and vancomycin is incorrect. Some units advocate giving vancomycin in addition to piperacillin/tazobactam if there is an indwelling central venous access device. This patient does not have such a device in situ and this procedure is not supported by NICE.

Piperacillin/tazobactam and gentamicin is incorrect. NICE specifically advise not adding an aminoglycoside unless local policy dictates.

Piperacillin/tazobactam and gentamicin and vancomycin is incorrect. This is not a treatment strategy supported by NICE.

Question 83 of 89

A 67-year-old woman presents to her GP with a lump in her armpit that she first noticed two months ago, and feels is getting bigger. She has not suffered from pyrexia, night sweats, weight loss or lethargy. The GP runs some blood tests, which can be seen below.

Hb	116 g/L	Male: (135-180)Female: (115 - 160)

Platelets	160 * 10 /L 9	(150 - 400)
WBC	72 * 10 /L 9	(4.0 - 11.0)
Neuts	5 * 10 /L 9	(2.0 - 7.0)
Lymphocytes	66 * 10 /L 9	(1.0 - 3.5)
Blood film	smudge cells	

Which of the following would imply a poor prognosis in this woman?

A. Female sex
B. Philadelphia translocation
C. Low B2-microglobulin
D. Del 17p
E. Age less than 70

D. Del 17p

del 17p is associated with a poor prognosis in CLL

This woman is suffering from chronic lymphocytic leukaemia (CLL), a slowly progressive disease. Most patients are either asymptomatic or present with lymphadenopathy. Only 10% of patients will have B symptoms of lymphoma. Half of the patients present with splenomegaly and about 15% with hepatomegaly. The key to making this diagnosis is the lymphocyte-predominant leukocytosis, with smudge cells on the blood film. Smudge cells, also known as smear cells, are cell remnants that arise during slide preparation and are the result of abnormally fragile lymphocytes in CLL.

From the options given above, the only poor prognostic indicator is del 17p mutation, which indicates resistance to standard chemotherapy regimens. B2-microglobulin levels are used in multiple myeloma where raised levels imply poor prognosis. It has also been included in the new (2016) CLL international prognostic index, where again high levels imply poor prognosis.

Philadelphia translocation, t(9;22), is a poor prognostic factor in ALL.Male sex, not female sex, is a poor prognostic factor.An age of fewer than 70 years old is a good prognostic marker

Question 84 of 89

A 16-year-old boy from Iran presents to the emergency department with dyspnoea, dry cough, and fevers.

On arrival, his oxygen saturations are 91% with a respiratory rate of 27/minute. His blood pressure is 110/70mmHg and heart rate 89/minute. There are widespread crackles on auscultation.

Chest x-ray shows diffuse bilateral interstitial infiltrates. You begin treatment for communityacquired pneumonia and send sputum samples for culture.

Blood tests:

Hb	95g/L	Male: (135-180)Female: (115 - 160)
Platelets	140* 10 /L 9	(150 - 400)
WBC	2.7* 10 /L 9	(4.0 - 11.0)
Neuts	0.7* 10 /L 9	(2.0 - 7.0)
Lymphs	1.7* 10 /L 9	(1.0 - 3.5)
Mono	0.1* 10 /L 9	(0.2 - 0.8)
Eosin	0.2* 10 /L 9	(0.0 - 0.4)
Na +	140mmol/L	(135 - 145)
K +	3.8mmol/L	(3.5 - 5.0)
Urea	9mmol/L	(2.0 - 7.0)
Creatinine	80µmol/L	(55 - 120)
CRP	234mg/L	(< 5)

His sputum sample grows *Pneumocystis jirovecii* and his antimicrobials are changed to include Cotrimoxazole.

You return to take a more detailed history. He denies any recent treatment with glucocorticoids or immunosuppressive agents. He denies intravenous drug use and informs you he is not yet sexually active. His mother is in attendance and tells you he has suffered from recurrent gastroenteritis throughout his childhood and she feels this led to him being smaller than his peers.

What is the most likely underlying unifying diagnosis?

A. Cryptosporidium
B. Hyper IgM syndrome
C. HIV
D. Acute lymphoblastic leukaemia
E. Malnutrition

A. Cryptosporidium

Hyper IgM syndrome characteristically presents with infections e.g. *Pneumocystis* pneumonia, hepatitis, diarrhoea

This patient has presented with pneumocystis pneumonia, an opportunistic infection caused by an underlying immune deficiency (hyper IgM syndrome).

Hyper IgM syndrome is a heterogeneous group of disorders characterised by defective classswitch recombination leading to raised serum IgM with low levels of IgG and IgA. The most common form is an X-linked recessive trait due to mutation of CD40LG gene affecting roughly 2/1,000,000 males. The mechanism involves impaired immune signalling between T and B cells leading to primary immune deficiency.

Hyper IgM typically presents in infancy as acute severe infection such as pneumocystis pneumonia or cryptosporidium. It may also present as chronic infections throughout childhood with failure to thrive. CMV is common and may lead to associated liver disease. It is also associated with increased risk of hepatocellular carcinoma, cholangiocarcinoma and neuroectodermal tumours. A minority of patients may present with autoimmune disease such as inflammatory bowel disease.

Acute lymphoblastic leukaemia is unlikely given the long history of recurrent infection. HIV is less likely as this patient denies any risk factors or exposure.

Cryptosporidium is an opportunistic infection and is commonly associated with hyper IgM syndrome. It is the likely causative organism for his recurrent gastroenteritis but does not explain his current presentation. Given the history of opportunistic infections, he should be investigated for causes of immunodeficiency.

Malnutrition is incorrect. Recurrent gastroenteritis in childhood may lead to malnutrition and secondary immunodeficiency. However, the question asks for an 'underlying unifying diagnosis'. This should include a cause for his history of recurrent gastroenteritis

Question 85 of 89

A 72-year-old woman presents to the emergency department with a painful and swollen leg. This has developed over two days, and she otherwise feels well in herself. She was recently away on holiday to Spain and returned four weeks ago. She is able to mobilise independently and has had no reduced periods of mobility. She has a background breast cancer diagnosed four years ago, which unfortunately relapsed and spread into her liver. She is now on hormonal treatment only.

On examination, her left leg is swollen and red, and the calf diameter is significantly larger on the left side. A doppler ultrasound scan demonstrates a left-sided deep vein thrombus.

What is the most appropriate anticoagulation strategy?

A. 2-4 months of low molecular weight heparin (LMWH)
B. 3-6 months of low molecular weight heparin (LMWH)
C. 3-6 months of a direct oral anticoagulant (DOAC)
D. Three months of warfarin
E. Six months of warfarin

3. 3-6 months of a direct oral anticoagulant (DOAC)

Cancer patients with VTE - 6 months of a DOAC

NICE updated their guidelines in 2020. DOACs are now preferred to LMWH for patients with active cancer.

As active cancer is likely to cause a continued pro-coagulopathic state, it is recommended to continue anticogulation for longer than the standard 3 months

. Question 86 of 89

A 52-year-old woman presents to her GP complaining of fatigue and bruising. She has no significant medical co-morbidities. She is referred to the haematology clinic after an abnormal full blood count. Blood results are as follows:

Hb	112 g/L	Male: (135 - 180)Female: (115 - 160)
Platelets	150 * 10 /L 9	(150 - 400)
WBC	25.3 * 10 /L 9	(4.0 - 11.0)
Neuts	4.0 * 10 /L 9	(2.0 - 7.0)
Lymphs	16.2 * 10 /L 9	(1.0 - 3.5)
Mono	3.0 * 10 /L 9	(0.2 - 0.8)
Eosin	1.1 * 10 /L 9	(0.0 - 0.4)
LDH	250 U/L	(140 - 280 U/L)

Multicolour flow cytometry assay reports CD20+, CD23+,and CD5+ expression. She also undergoes fluorescence in situ hybridization (FISH) which reveals a deletion in the short arm of chromosome 17.

Which of the following features in this case is associated with a poor prognosis?

A. Age
B. FISH result
C. Flow cytometry assay result
D. Gender
E. LDH level

B. FISH result

del 17p is associated with a poor prognosis in CLL

The high white cell count composed mostly of lymphocytes points towards a diagnosis of chronic lymphocytic leukaemia (CLL). In CLL, deletion (del) of the short arm of chromosome 17 (17p) is found in under 10% of patients. This abnormality is associated with rapid progression of the disease, as well as a poor response to treatment strategies.

Prognosis is less favourable in those who are over the age of 70, rather than younger patients like this one.CD20+, CD23+, and CD5+ are surface antigens that are expressed in most CLL cases and shouldn't affect prognosis.Male sex, rather than female sex, is associated with a poor prognosis in CLL.Raised LDH is a marker for poor prognostic outcome, but it is normal in her case.

Question 87 of 89

An 18-year-old woman attends the emergency department with difficulty breathing.

On examination, she is cyanosed, her oxygen saturations are 84% on a finger probe, and her chest is clear.

She tells you that she has had a blue tinge around her mouth for her whole life and that she did have some investigations abroad before moving to the UK aged 4.

You take a blood gas, the sample is a dark brown colour. The results are as follows:

pH	7.35	7.35-7.45
PaCO2	4.5kPa	4.7 - 6.0
PaO2	12kPa	11 - 13

Given the likely diagnosis, what is the treatment of choice for the underlying condition?

A. 15L oxygen via a non-rebreathe mask
B. Ascorbic acid
C. Hyperbaric oxygen
D. IV methylthioninium chloride
E. Nitric oxide

B. Ascorbic acid

Ascorbic acid is the treatment of choice for NADH methaemoglobinaemia reductase deficiency

The chocolate brown blood sample, normal PaO2 but low oxygen saturations, and persistent cyanosis since childhood all point towards methaemoglobinaemia. Congenital NADHmethaemoglobinaemia reductase deficiency is usually diagnosed in childhood presenting withpersistent cyanosis with or without shortness of breath.Ascorbic acid is the correct answer, it is the treatment of choice for NADH methaemoglobinaemiareductase deficiency. **15L oxygen via a non-rebreathe mask** is incorrect. This patient may very well have 15L oxygen via a non-rebreathe mask applied in the emergency setting due to the low oxygen saturations, but this would not be the treatment for the underlying condition.

Hyperbaric oxygen is incorrect, this would be a treatment option for carbon monoxide poisoning.

IV methylthioninium chloride is incorrect, it would be the treatment of choice for acquired methaemoglobinaemia rather than congenital.

Nitric oxide is incorrect, this is actually a cause of acquired methaemoglobinaemia.

Question 88 of 89

An 83-year-old woman is seen in clinic by her oncologist. She has recently been diagnosed with chronic lymphocytic leukaemia (CLL). Her blood tests and clinical picture are stable and therefore she is being monitored and treatment has not been initiated. She is to undergo genetic testing to assess her prognosis.

Which of the following is associated with a poor prognosis in her condition?

A. IGHV mutation
B. t(8;21)
C. Trisomy 8
D. t(9;22)
E. del 17p

A. del 17p

del 17p is associated with a poor prognosis in CLL

In chronic lymphocytic leukaemia, del 17p is a poor prognostic factor. IGHV is associated with a good prognosis in CLL rather than a poor one. t(8;21) is associated with a good prognosis in acute myeloid leukaemia. Trisomy 8 is a poor prognostic factor in acute lymphoblastic leukaemia. It is very rarely found in CLL and the prognostic relevance is unknown. t(9:22) is the Philadelphia chromosome and is part of the diagnostic criteria for chronic myeloid leukaemia and carries a poor prognosis in acute lymphocytic leukaemia

Question 89 of 89

A 41-year-old patient receiving treatment for breast cancer presents to the Day Unit with a swollen right leg. She had a left mastectomy and axillary clearance 3 months ago and is currently receiving her second cycle of FEC (epirubicin, cyclophosphamide and fluorouracil) chemotherapy. Ultrasound doppler confirms a deep vein thrombosis of the right superficial femoral vein. The patients renal function is normal.

What is the most appropriate treatment for this patient?

A. Rivaroxaban for 4-6 weeks and reassess VTE risk
B. Warfarin for six months and reassess VTE risk
C. Rivaroxaban for 3-6 months and reassess venous thromboembolism (VTE) risk
D. Warfarin for 3 months and reassess VTE risk
E. Low molecular weight heparin for for 4-6 weeks and reassess VTE risk

C. Rivaroxaban for 3-6 months and reassess venous thromboembolism (VTE) risk

Cancer patients with VTE - 6 months of a DOAC

This patient is receiving treatment for active cancer. NICE guidance recommends that patients with active cancer and venous thromboembolism (VTE) should receive 3-6 months treatment with a direct oral anticoagulant such as rivaroxaban. Their risk of further VTE should then be reassessed and a decision made by the clinical team regarding ongoing VTE treatment or prophylaxis. Previously it was recommended that low-molecular weight heparin was used in this scenario.

Warfarin is avoided in patients with active cancer due to interaction with medications; the need for treatment pauses if patients become pancytopenic and increased bleeding risk.

ONCOLOGY

passmedicine PART 2

2024

Question 1 of 43

A 20-year-old asymptomatic woman is referred to the genetics clinic. Her grandmother died of breast cancer aged 54 and her mother and older sister have both recently been diagnosed with the disease.

Breast examination does not reveal any lumps and her recent ultrasound of the breasts did not reveal any suspicious lesions.

What should she be told about her breast cancer risk?

A. Her chance of having a BRCA1 mutation is 55-65%

B. Her chance of having a BRCA2 mutation is 55-65%

C. If BRCA1 positive, she has a 55-65% chance of developing breast cancer

D. If BRCA2 positive, she has a 55-65% chance of developing breast cancer

E. Given her family history, she has a 55-65% chance of developing breast cancer

C. If BRCA1 positive, she has a 55-65% chance of developing breast cancer

The BRCA1 and BRCA2 genes are tumour suppressor genes involved in DNA repair. Familial mutations in these genes are associated with an increased risk of breast and ovarian cancer. Carriers tend to develop these cancers at a younger age as they have an inherited germline mutation of one copy of the gene so only require a 'second hit' of damage to the second copy to inactivate it. BRCA mutations account for 20-25% of hereditary breast cancers and 5-10% of all breast cancer cases, They also account for 15% of all ovarian cancer.

If a woman with at least a 10% risk of breast or ovarian cancer (approximated from family history) will be offered genetic screening. This requires genetic counselling and living relative whose DNA can also be tested for the mutation, otherwise, the chance of identifying the mutation is too low. This has important ethical considerations with regard to consent.

The percentage risk of developing breast cancer by age 70 is 55-65% for BRCA1 and 45% for BRCA2 mutations.

The percentage risk of developing ovarian cancer by age 70 is 40% for BRCA1 and 15% for BRCA2 mutations.

Because of the high risks involved, women with a positive test result may choose to have enhanced screening for these cancers, prophylactic surgery (bilateral mastectomy and/or bilateral salpingo-oophorectomy) or chemoprevention with hormonal drugs.

Question 2 of 43

You are working as a registrar on the palliative care ward. A 58-year-old lady is admitted for symptom control. She has a past medical history of metastatic pancreatic cancer and diabetic nephropathy. She has been suffering from severe abdominal pain which has been unresponsive to titration of morphine, gabapentin and duloxetine.

Blood results are as follows:

Hb	75 g/l	Na +	138 mmol/l
Platelets	224 * 10 /l 9	K +	3.8 mmol/l
WBC	14.9 * 10 /l 9	Urea	18.6 mmol/l
Neuts	12.9 * 10 /l 9	Creatinine	288 µmol/l
eGFR	22 mL/min		

You decide to start an opioid which acts as a neuropathic agent by NMDA antagonism. What analgesic is most appropriate?

A. Methadone

B. Oxycodone

C. Buprenorphine

D. Paracetamol

E. Venlafaxine

A. Methadone

Methadone can be used as a third line opioid for patients with complex pain that is poorly responsive to other opioids and adjuvants

Methadone can be used as a third line opioid for patients with complex pain that is poorly responsive to other opioids and adjuvants. The patients pain has not responded to titration of morphine, combined with two neuropathic adjuvants. Methadone should therefore be considered.

The patients eGFR is les than 30 which also strengthens the decision to start methadone. Opioids which are safe in CKD 4 and 5 include fentanyl, buprenorphine and methadone.

Paracetamol and venlafaxine are not opioids.

Question 3 of 43

You are asked to provide advice on a patient who has metastatic renal cell carcinoma with pulmonary and bone metastases. They are being managed in their own home with community palliative care input, but their swallow has started to deteriorate. It is now felt that they are approaching the terminal phase of their illness and a decision has been made to start a syringe driver. They report good pain control with their current analgesia regime.

Their current analgesia regime is 60mg oxycodone modified release capsules twice a day with oxycodone instant release, taken as required. The oxycodone modified release is converted into the equivalent subcutaneous dose for an oxycodone syringe driver.

What would be the most appropriate dose of breakthrough analgesia to prescribe based on the current syringe driver dose?

A. Oxycodone I/R oral solution 20mg

B. Oxycodone I/R oral solution 10mg

C. Oxycodone subcutaneous injection 10mg

D. Morphine sulphate for injection 10mg

E. Morphine sulphate injection 20mg

C. Oxycodone I/R oral solution 10mg

Breakthrough dose = 1/6th of daily morphine dose

The breakthrough dose for analgesia should be one sixth of the total dose administered within 24 hours. If there are no changes to the total dose of oxycodone and it is converted to subcutaneous then the total dose is halved (120mg to 60mg). This is because the subcutaneous strength is twice that of oral oxycodone. The drug choice for breakthrough should match what is in the syringe driver as much as possible (stick with oxycodone) and the breakthrough should be a sixth of the total dose. Given that they need a syringe driver which is made up of oxycodone, the most appropriate drug choice would be subcutaneous oxycodone. Therefore, the breakthrough dose would be a sixth of 60mg= 10mg.

Question 4 of 43

You are looking after a 65-year-old man with a background of high-grade lymphoma who she is currently receiving R-CHOP chemotherapy for. She developed neutropaenic sepsis yesterday for which she was started on piperacillin/tazobactam, and gentamicin. She has been persistently pyrexial for the past 24 hours.

She has a background of complex pain for which she uses a 25micrograms/hour fentanyl patch. You are asked to review her due to confusion and visual hallucinations. On examination, she has pinpoint pupils, GCS 14 (M6, V4, E4), and you note myoclonic jerks.

Na +	136 mmol/L	(135 - 145)
K +	3.8 mmol/L	(3.5 - 5.0)
Bicarbonate	19 mmol/L	(22 - 29)
Urea	7.2 mmol/L	(2.0 - 7.0)
Creatinine	130 µmol/L	(55 - 120)
Bilirubin	14 µmol/L	(3 - 17)
ALP	95 u/L	(30 - 100)
ALT	82 u/L	(3 - 40)
Î³GT	86 u/L	(8 - 60)
Albumin	35 g/L	(35 - 50)

You suspect opioid toxicity. What is the most likely explanation for this?

A. Acidosis

B. Fentanyl and piperacillin/tazobactam drug interaction

C. Increased fentanyl absorption due to pyrexia

D. Liver dysfunction

E. Renal dysfunction

C. Increased fentanyl absorption due to pyrexia

Transdermal fentanyl absorption is increased by heat (e.g. hot water bottle) or pyrexia, potentially leading to opioid toxicity

Transdermal fentanyl absorption is increased by heat or pyrexia (which results in vasodilation and increased blood flow), potentially leading to opioid toxicity. This is therefore the correct option.

Acidosis is incorrect. Acidosis is not known to exacerbate opioid toxicity.

Renal dysfunction is incorrect. Fentanyl is hepatically metabolised by CYP450 3A4 with no active metabolites. Therefore it is the opioid of choice in renal failure.

Liver dysfunction is incorrect. Although the patient has a mild transaminitis, their synthetic liver function is normal, making it an unlikely contributing factor.

Piperacillin/tazobactam is incorrect. Fentanyl has no known interactions with piperacillin/tazobactam.

Question 5 of 43

A 63-year-old woman presents with unrelenting thoracic back pain. She finds that the pain is debilitating, especially as she helps look after her grandchildren. She has a past medical history of breast cancer diagnosed two years ago, for which she underwent a mastectomy with reconstruction. She also had postoperative radiotherapy and endocrine therapy. As she was found to be BRCA1 positive, she underwent a hysterectomy with bilateral oophorectomy as well. On examination, she is tender over the spine at T4, but neurological examination is unremarkable.

What is the most appropriate imaging investigation for her back pain?

A. MRI of the whole spine within 7 days

B. MRI of the thoracic spine within 7 days

C. MRI of the whole spine within 24 hours

D. MRI of the thoracic spine within 24 hours

E. Bone scan of the whole body within 7 days

A. MRI of the whole spine within 7 days

The correct answer is MRI whole spine within 7 days. This is a patient with known cancer presenting with highly suspicious back pain but no evidence of spinal cord compression. The most appropriate modality is MRI which can not only detect metastasis but also demonstrate patency or compression of the spinal cord. The whole spine should be scanned as to exclude further metastasis as 30-50% of patients have multi-level involvement by the time of presentation. The timing of the scan depends on suspicion of cord

compression. For this patient, there is no evidence of neurological compromise and therefore the scan does not have to occur within 24 hours.

Question 6 of 43

You are looking after a 68-year-old man with aggressive multiple myeloma. He has intractable vomiting which has not improved with regular subcutaneous metoclopramide.

Blood results are as follows:

Calcium	4.2 mmol/L	(2.1-2.6)

You decide to start him on a syringe driver. What would be your anti-emetic of choice?

A. Aprepitant

B. Cyclizine

C. Levomepromazine

D. Nabilone

E. Ondansetron

C. Levomepromazine

Metabolic causes of nausea and vomiting, for example uraemia and hypercalcaemia, cause nausea and vomiting by stimulating dopamine type 2 (D2) receptors on the chemoreceptor trigger zone. This pathway is most effectively blocked by using a central dopamine antagonist such as haloperidol

Metabolic causes of nausea and vomiting (e.g. hypercalcaemia) are particularly sensitive to central dopamine antagonists such as **levomepromazine** making this the favoured choice.

Levomepromazine is a very broad spectrum anti-emetic that acts as an antagonist to multiple receptors including histamine type 1, muscarinic-cholinergic, dopaminergic 2, alpha-1 adrenoceptor, and 5HT-2 receptors. Thus it is a powerful anti-emetic that can be used in many scenarios.

Aprepitant is a substance P/neurokinin 1 receptor antagonist used to prevent chemotherapyinduced and postoperative nausea and vomiting. The patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Cyclizine is a histamine H1-receptor antagonist which may have effects directly on the vestibular system and on the chemoreceptor trigger zone. It also exerts a central anticholinergic action The patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Ondansetron is a specific 5HT3-receptor antagonist which blocks 5HT3 receptors in the gastrointestinal tract and in the CNS. The patient in this clinical case has nausea secondary to a metabolic abnormality, and thus a dopamine antagonist is the preferred choice.

Nabilone is a synthetic cannabinoid which is used to treat nausea and vomiting caused by cytotoxic chemotherapy, which is unresponsive to conventional antiemetics.

Question 7 of 43

A 54-year-old-man with a history of granulomatosis with polyangiitis attends for his annual review in the rheumatology clinic. He was diagnosed at age 35 where he presented with rapidly progressive glomerulonephritis and pulmonary haemorrhage and was treated with cyclophosphamide and steroids. He required a period of haemofiltration on the intensive care unit but has remained well since.

Today, he feels well after recently quitting smoking but reports occasional blood in his urine. On examination, his abdomen is soft and non tender, there is no pallor or oedema and his chest is clear. His investigations are below and his urine appears clear.

Hb	105 g/l
Platelets	300* 10 /l9
WBC	5* 10 /l9
Urinalysis	blood 3+ protein -
Na +	139 mmol/l
K +	4.2 mmol/l
Urea	5.6 mmol/l
Creatinine	98 µmol/l

What is his likely diagnosis?

A. Recurrence of glomerulonephritis

B. Transitional cell carcinoma

C. Renal calculi

D. Faulty urinalysis recording

E. Rhabdomyolysis

B. Transitional cell carcinoma

Use of cyclophosphamide in granulomatosis with polyangiitis is associated with increased risk of bladder cancer

The use of cyclophosphamide is linked to transitional cell carcinoma in patients with vasculitis. Given that his U&Es are normal, a recurrence of glomerulonephritis is unlikely. Renal calculi would cause loin to groin pain. Haematuria can often not be visible to the eye even when present. While rhabdomyolysis could give a positive dipstick, there are no other features to suggest this

Question 8 of 43

A 68-year-old man is admitted to the unit with an exacerbation of severe pain around his abdomen. He describes it as a tight band like pain which is burning in character. He has a past medical history of metastatic prostate cancer. His drug history includes morphine modified release (100mg, twice daily), duloxetine (60mg, twice daily), pregabalin (200mg, three times per day). He states that the pain initially responded well to the analgesics he is on however over the past few weeks it has got progressively worse and culminated in a severe attack of pain today.

You suspect that he has got severe neuropathic pain secondary to spinal metastases. The pain is now poorly controlled with a large dose of opioids and two neuropathic agents. Your consultant decides to start him on ketamine.

What acute complication is it important to monitor for?

A. Bladder dysfunction

B. Liver dysfunction

C. Raised intracranial pressure

D. Cardiomyopathy

E. Pulmonary fibrosis

C. Raised intracranial pressure

Ketamine can cause raised intracranial pressure. It is important to monitor for side effects such as headache, papilloedema, and vomiting

Ketamine can be used for neuropathic pain poorly responsive to titrated opioids and oral adjuvant analgesics (e.g. antidepressant and/or anticonvulsant) particularly when there is abnormal pain sensitivity (e.g. allodynia, hyperalgesia or hyperpathia). Ketamine is an NMDA receptor antagonists. Side effects to be aware of include hypertension, raised intracranial pressure and hallucinations.

Bladder and liver dysfunction can occur with long term use of ketamine. Therefore, if a patient is anticipated to have a reasonably good prognosis, alternative options should be considered to replace the ketamine, for example lidocaine infusions.

Question 9 of 43

A medical consult was sought from the nursing staff concerning a 68-year-old gentleman admitted with a urinary tract infection. He was diagnosed with terminal adenocarcinoma of the pancreas six months ago. He had complained of increasing severe abdominal pain for the last few weeks for which his GP commenced and then titrated morphine sulphate tablets (MST) achieving a temporary analgesic effect with each increment. By the time of admission he had been using 150mg BD and was unable to tolerate any further dose increases owing to drowsiness.

His drug history comprised of ciprofloxacin 250mg BD started four days ago for the management of urinary tract infection, paracetamol 1g QDS, tramadol 100mg QDS, MST 150mg BD, senna 2 tabs ON & Movicol one sachet BD.

In view of the continuing abdominal pain investigations were organised by the inpatient team revealing the following findings:

Hb	135 g/l
Platelets	224 * 10 /l9
WBC	11.2 * 10 /l9
Bilirubin	23 µmol/l
ALP	189 u/l
ALT	326 u/l
γGT	178 u/l
Albumin	34 g/l

Chest x-ray: Normal heart borders and lung fields, no evidence of subdiaphragmatic air. Abdominal x-ray: presence of faeces, no evidence of dilatation.

USS abdomen: multiple hypoechoic lesions within the liver, nil else abnormal noted. What is the next most appropriate management option?

A. Commence syringe driver containing diamorphine

B. Refer for immediate surgical consult

C. Refer for palliative radiotherapy

D. Convert MST to fentanyl

E. Commence trial with dexamethasone

E. Commence trial with dexamethasone

This gentleman has evidence of extensive hepatic metastases most probably arising from known adenocarcinoma of the pancreas. Despite an escalating opiate regimen he is unable to obtain satisfactory pain relief. One of the sources of pain associated with liver metastases is due to stretching and irritation of the liver capsule for which a trial of dexamethasone may provide an analgesic effect. Option 5 is, therefore, the most suitable option.

There is no evidence of obstruction or perforation and thus a surgical consult is not warranted, and palliative radiotherapy is not specifically indicated here (in contrast with bone metastases).

Switching to fentanyl will probably not provide any additional benefit in terms of tolerance compared with MST; it is however indicated in patients with poor renal failure owing to its predominant hepatic route of metabolism. For further information:

Question 10 of 43

A medical consult was sought regarding a 58-year-old gentleman admitted with pneumonia complaining of relentless hiccups. He was diagnosed with hepatocellular carcinoma six months ago and was deemed not for curative treatment owing to the extent of the disease. He was initially comfortable with no discernible symptoms but over the last four weeks developed hiccups. In conjunction with the palliative care nurse his GP had initially trialled domperidone and then haloperidol but with no improvement in his symptoms. He denied the presence of any other symptoms other than fatigue, and upon questioning denied the presence of abdominal pain, heartburn or early satiety.

His past medical history was comprised of alcohol dependence syndrome, chronic liver disease, hypertension and hypercholesterolaemia for which he was prescribed thiamine 100mg TDS, lactulose 10mls BD, spironolactone 100mg OD, propranolol 40mg OD, simvastatin 20mg OD as well as intravenous co-amoxiclav 625mg TDS for the treatment of his pneumonia. Examination revealed the presence of a cachectic male. His blood pressure was 108/58 mmHg, heart rate 78 bpm, respiratory rate 18/min and temperature 36.6ºC. Examination of his gastrointestinal system revealed the presence of a palpable mass in the right upper quadrant inferior to the right sterna edge and ascites with no tenderness. Examination of his neurological system revealed the absence of any focal neurological symptoms; likewise, examination of cardiovascular and respiratory systems was unremarkable.

Recent investigations revealed the following results:

Bilirubin	22 µmol/l
ALP	221 u/l
ALT	278 u/l
Protein	62 g/l
Albumin	18 g/l

Chest x-ray: normal heart borders and lung fields

Surveillance upper GI endoscopy four months ago: normal stomach mucosal surface, no evidence of portal hypertension

Which of the following options is the best option with a view to managing his hiccups?

A. Commence treatment with proton pump inhibitor

B. Commence treatment with levomepromazine

C. Commence treatment with dexamethasone

D. Commence treatment with midazolam infusion

E. Commence treatment with baclofen

C. Commence treatment with dexamethasone

This gentleman has known advanced hepatocellular carcinoma and is complaining of distressing hiccups. He does not have any sign of gastro-oesophageal reflux and therefore a trial of proton pump inhibitor is unlikely to be of benefit. In the presence of hepatic or cerebral cancer a trial of dexamethasone may induce some remission and is therefore suggested as an appropriate next line given he has already had a trial of treatment with a prokinetic and a typical antipsychotic with no remission; see http://www.palliativecareguidelines.scot.nhs.uk/guidelines/symptomcontrol/Hiccups.aspx for further information. There is also limited evidence for treatment with baclofen and levomepromazine; subcutaneous midazolam should be reserved if all else proves futile. Note also the BNF has a very useful section regarding prescribing in palliative care scenarios; in this instance it also suggests the use of antacids or nifedipine in addition to the above options.

Question 11 of 43

A 47-year-old woman presents to the emergency department with sudden onset of shortness of breath and pleuritic chest pain. Observations demonstrate marked hypoxia and she is given oxygen and analgesia and undergoes a chest X-ray followed by a CT pulmonary angiogram which shows a pulmonary embolism. There is also an incidental finding of a nodule suspicious of metastatic disease.

She is started on a treatment dose of low molecular weight heparin and admitted under the medical team for further assessment. During a more detailed history, she explains that she has lost one stone in weight over two months and been feeling progressively more tired as well. She denies any other symptoms. She has a past medical history of asthma and also underwent a caesarean section three years ago. She has two children, of which she breastfed both, and has a long history of use of oral contraceptive use. She is an ex-smoker of 5 pack-years and has minimal alcohol intake. Her grandfather died of prostate cancer, and her sister developed breast cancer at the age of 52.

A complete further examination was completed and no abnormalities were found. Routine blood tests are currently pending, and a flexible bronchoscopy for biopsy of the lung nodule has been arranged.

How should this patient be further investigated?

A. Tumour markers AFP and hCG, and mammography

B. CT abdomen and pelvis, tumour markers AFP and hCG, and a myeloma screen

C. Ultrasound abdomen and pelvis, and tumours marker AFP and hCG

D. CT abdomen and pelvis, and tumour markers AFP and hCG

E. CT abdomen and pelvis, myeloma screen, and colonoscopy

D. CT abdomen and pelvis, and tumour markers AFP and hCG

The correct answer is CT abdomen and pelvis, and tumour markers AFP and hCG. These investigations complete all those recommended by NICE for an unknown primary. This question highlights how to investigate a malignancy of unknown origin. This patient has a likely metastatic disease causing a pulmonary embolism with unclear clinical findings as to the location of the primary malignancy.

NICE recommends the following investigations for all patients:

- FBC, U&E, LFT, calcium, urinalysis, LDH
- Chest X-ray
- CT of chest, abdomen and pelvis
- AFP and hCG

NICE recommends the following investigations for specific patients:

- Myeloma screen (if lytic bone lesions)
- Endoscopy (directed towards symptoms)
- PSA (men)
- CA 125 (women with peritoneal malignancy or ascites)
- Testicular US (in men with germ cell tumours)
- Mammography (in women with clinical or pathological features compatible with breast cancer)

A is incorrect because it does not include CT scanning of the abdomen and pelvis. Mammography is tempting but NICE does not recommend it without any clinical findings which are suggestive of a breast malignancy. B and E are incorrect because a myeloma screen is not indicated without lytic bone lesions. E is also incorrect as colonoscopy should be symptom directed. C is incorrect as US is not an appropriate investigation.

Question 12 of 43

A 62-year-old lady with metastatic breast cancer is admitted with a general decline. She is found to have a pneumonia and treated with IV fluids and antibiotics. She makes limited improvement with these and antibiotics are stopped. The decision is made to focus on control of her symptoms.

She is started on a syringe driver of morphine sulphate to treat breathlessness and pain related to liver metastases. She then develops nausea and hiccups.

Which medication is the best choice to add to the syringe driver?

A. Cyclizine

B. Domperidone

C. Midazolam

D. Metoclopramide

E. Ondansetron

D. Metoclopramide

Cyclizine, domperidone and ondansetron are anti-emetics, though domperidone does not come in a subcutaneous preparation for syringe driver. Midazolam is an anxiolytic.

Metoclopramide is the first choice to treat hiccup as well as nausea. Other options include baclofen, nifedipine and chlorpromazine.

Question 13 of 43

A 60-year-old man has been admitted under urology with difficulty passing urine and back pain. A post-void bladder scan shows 980mls in his bladder. He was catheterised by the admitting doctor and now has haematuria.

He has a background of metastatic prostate cancer, atrial fibrillation, previous NSTEMI, hypertension, hypercholesterolaemia and hypothyroidism. His medications include warfarin and modified-release morphine 30mg every 12 hours.

He has been seen by the urology consultant who has said to put a 3-way catheter in if the haematuria does not settle and refer to the palliative care team for pain management. The palliative care specialist advised increasing the modified release morphine to 45mg every 12 hours.

What dose of immediate-release morphine should the patient be prescribed for breakthrough pain?

A. 5mg

B. 7.5mg

C. 10mg

D. 15mg

E. 20mg

D. 15mg

Breakthrough dose = 1/6th of daily morphine dose

To answer this question, you need to calculate the total daily dose of morphine. The amount of immediate-release morphine for breakthrough pain should be one-sixth (1/6) of the total daily dose.

The patient was previously on 60mg of morphine per day. One-sixth of this would be 10mg of immediate-release morphine for breakthrough pain.

The modified release morphine has now been up titrated to 90mg per day. Whenever background morphine is increased, it is important to calculate the new breakthrough pain dosage for patients to receive the maximal benefit. In this case, one-sixth of 90 is 15mg. Therefore the correct answer is 15mg of immediate-release morphine.

Question 14 of 43

You are looking after an 82-year-old man with a background of metastatic colorectal carcinoma. He is in significant pain and is on a syringe driver containing 6mg of alfentanil. He has end-stage renal failure.

What breakthrough analgesic will you prescribe?

A. 1mg subcutaneous alfentanil

B. 25mg subcutaneous morphine

C. 25mg subcutaneous oxycodone

D. 2mg subcutaneous alfentanil

E. 50mg subcutaneous oxycodone

A. 1mg subcutaneous alfentanil

Breakthrough dose = 1/6th of daily morphine dose

Palliative care guidelines recommend using 1/6 of the daily dose as a breakthrough. Alfentanil is a potent drug and is particularly useful in renal failure as it is metabolised by the liver, has no active metabolites, and has a very short half-life.

Question 15 of 43

An 82-year-old man is reviewed by the palliative care team on the ward. He has a past medical history of metastatic lung cancer. He is not for any further chemotherapy, surgery or radiotherapy. He has deteriorated rapidly in the prior few days and is considered to be in the last days of life. He is suffering from intractable nausea, the cause of which is not clear.

What is the most appropriate medication to manage his symptoms?

A. Buscopan

B. Levomepromazine

C. Metoclopramide

D. Morphine

E. Ondansetron

B. Levomepromazine

Levomepromazine is a 'dirty drug' which blocks lots of different receptors (e.g. ACh, DA, 5HT). It is therefore a broad spectrum anti-emetic. It is first line in the last days of life.

Levomepromazine is correct. This is a broad-spectrum anti-emetic - a 'dirty drug' targeting many receptors. It is therefore the most suitable choice where the cause of nausea is unknown and in the last days of life.

Buscopan is incorrect. This is indicated in palliative care for excess secretions rather than nausea.

Metoclopramide is incorrect. This would be a rational choice for nausea due to gastric stasis. However, where the cause is unknown and in the last days of life, a more broad spectrum antiemetic is preferred. Therefore, levomepromazine is preferable.

Morphine is incorrect. This is indicated in palliative care for breathlessness and pain rather than nausea.

Ondansetron is incorrect. This is a rational choice for chemotherapy or post-operative related nausea. However, it is a specific serotonin 5-HT3 receptor antagonist, with a low affinity for dopamine receptors and therefore has a more narrow spectrum of action than levomepromazine and is, therefore, less preferable in this circumstance.

Question 16 of 43

A 65-year-old woman presents to the emergency department with reduced consciousness. Her husband reports that she has been unwell for the past 3 days with coryzal symptoms. She has a past medical history of hypertension and metastatic pancreatic cancer for which she is under the palliative care team. Her regular medications include amlodipine, bisoprolol, paracetamol and a fentanyl patch for pain.

On examination, her temperature is 38.1ºC with a heart rate of 101 beats/min and a blood pressure of 118/66mmHg. Auscultation of the chest is clear with a respiratory rate of 8 breaths/min and oxygen saturations of 92% on air. Her abdomen is soft and non-tender and she is visibly jaundiced. She has a GCS of 11/15 (E2V4M5).

What is the most likely cause of this patient's reduced consciousness?

A. Delirium
B. Hepatic encephalopathy
C. Hypoglycaemia
D. Meningitis
E. Opioid toxicity

E. Opioid toxicity

Transdermal fentanyl absorption is increased by heat (e.g. hot water bottle) or pyrexia, potentially leading to opioid toxicity

Opioid toxicity is correct. This patient has signs of opioid toxicity including drowsiness and a slow respiratory rate. There are multiple differential diagnoses for an acutely unresponsive patient and, therefore, it is key to take a thorough history and examination. From this patient's collateral history it is learned that she uses a fentanyl patch for pain control. It is important to note that transdermal fentanyl absorption is increased by heat whether that be secondary to the application of a hot water bottle or pyrexia. This patient has a fever of 38.1ºC which is a likely contributing factor to her toxicity.

Delirium is incorrect. This is a very reasonable differential diagnosis given the history of fever in a patient with a frail comorbid status. However, delirium is less likely to cause this patient's reduced respiratory rate compared to opioid toxicity. Generally, fever is associated with tachypnoea and the opposite response should raise suspicion.

Hepatic encephalopathy is incorrect. Although this patient is jaundiced, it is likely to be cholestatic jaundice secondary to the underlying malignancy rather than decompensated liver disease. Furthermore, the acute onset of symptoms and lack of signs of hepatic encephalopathy makes the diagnosis less likely.

Hypoglycaemia is incorrect. This is an important differential diagnosis given the history of advanced malignancy and the likelihood of reduced oral intake. However, the presence of bradypnoea and opioid use makes opioid toxicity more likely.

Meningitis is incorrect. Fever and reduced consciousness are features of meningitis. However, the presence of bradypnoea and the use of strong opioid analgesics make opioid toxicity more likely.

Question 17 of 43

A 56-year-old man with metastatic small cell lung carcinoma is admitted to hospital with vomiting, ankle swelling and pruritus. He recently completed a course of palliative chemotherapy. He has a background of chronic obstructive pulmonary disease and hypertension and takes morphine sulphate (MST) for pain relief.

On examination, he is cachectic with peripheral oedema and skin excoriations. Heart rate is 96 beats per minute and blood pressure is 140/85 mmHg.

Tests show:

Hb	134 g/l
Platelets	185 * 10 /l9
WBC	5.5 * 10 /l9
Na +	146 mmol/l
K +	5.4 mmol/l
Urea	23 mmol/l
Creatinine	420 µmol/l
Urine dip:	Blood +
Urine osmolality	350 mOsm/L
Urinary sodium	45 mEqL
Microscopy:	red cells; casts.

What is the most appropriate pain relief for this patient?

A. Fentanyl patch
B. Diamorphine
C. Oxycodone
D. Pregabalin
E. Tramadol

A. Fentanyl patch

This patient has an acute kidney injury secondary to cisplatin chemotherapy. As a result, he needs adjustments to his pain relief. He is on regular, long-acting MST, so the most appropriate substitution is a fentanyl patch.

Oxycodone can be used in moderate renal failure, but only as breakthrough pain relief. Modified release preparations should be avoided. Diamorphine and tramadol should be avoided in renal failure. Pregabalin can be administered at reduced dose, but would not be an appropriate first-line substitution for MST.

Alfentanil and methadone are safe even in severe renal impairment and are administered subcutaneously. Alfentanil would be appropriate for this patient if he had unstable pain and required dose titration.

Question 18 of 43

A 69-year-old male patient presents with worsening mouth soreness and painful swallowing, progressively getting worse over the last week. He started radical radiotherapy for a base of mouth squamous cell cancer three weeks ago. He also has a PEG in situ. He was recently seen by the dietician and is now having fluid and Ensure nutritional supplements via his PEG. He had been given soluble paracetamol by the specialist nurse, but this has failed to control his pain.

On examination, his oral cavity appears inflamed with multiple small ulcers posterior to his lower lip. There are no patches or plaques inside. You change the paracetamol to liquid co-codamol and give him a topical lidocaine gel at 2% strength.

What is the most appropriate next step in management to control his symptoms?

A. Benzydamine mouthwash
B. Menthol mouthwash
C. Chlorhexidine mouthwash
D. Fluconazole
E. Metronidazole

A. Benzydamine mouthwash

The correct answer is benzydamine mouthwash. This gentleman is suffering from radiotherapyinduced mucositis. Given the location of his tumour and the high dose of radiotherapy necessary for curative therapy, mucositis is not an uncommon side effect. Many of these patients will have a PEG inserted prophylactically in anticipation of the difficulties in maintaining an oral diet with mucositis and oesophageal involvement. For this patient, already on co-codamol, benzydamine mouthwash can be very helpful in treating his symptoms. Menthol and chlorhexidine mouthwashes, often bought over the counter, would increase oral irritation. There is no evidence of fungal or bacterial infection currently.

Question 19 of 43

A 75-year-old man is admitted to the palliative care unit for end of life care. He has a past medical history of metastatic prostate cancer. His drug history includes a syringe driver with morphine, levomepromazine and midazolam. During personal care the nurses have stated that he suffers excruciating pain when being turned onto his side. His pain throughout the day is otherwise well controlled.

What is the most appropriate way to manage his pain?

A. Titrate the syringe driver morphine
B. Morphine sulphate modified release tablets
C. Oxycodone modified release tablets
D. Morphine sulphate immediate release liquid
E. Paracetamol

D. Morphine sulphate immediate release liquid

Incident pain is defined as pain which comes on as a result of an action or activity, for example during personal care. Sublingual fentanyl has rapid onset and is a short-acting opioid, and is therefore a good choice for treating this type of pain

Incident pain is defined as pain which comes on as a result of an action or activity, for example during personal care. Sublingual fentanyl has rapid onset and is a short-acting opioid, and is therefore a good choice for treating this type of pain. Similarly, morphine sulphate immediate release liquid is also suitable.

The patients pain during the day is otherwise well controlled therefore titrating up the syringe driver with more morphine is not appropriate. Not only will this not be particularly effective at treating the incident pain, it will also give rise to unnecessary side effects such as sedation and constipation.

Similarly, morphine sulphate modified release tablets have an action time of approximately 12 hours so they are therefore inappropriate for breakthrough pain as they will cause accumulation of morphine in the system predisposing to toxicity.

Question 20 of 43

A 64-year-old cachectic lady presents to the emergency department with difficulty in breathing. She reports smoking since she was 14 years old. Chest X-Ray reveals a large right sided pleural effusion. A sample is obtained under ultrasound-guidance for evaluation. CT does not identify a cause. The results of the pleural aspiration demonstrate an exudative effusion and histology is suggestive of an adenocarcinoma with positive TTF-1 stain.

What is the most likely cause for the effusion?

A. Non-small cell lung cancer
B. Small cell lung cancer
C. Ovarian carcinoma
D. Breast carcinoma
E. Mesothelioma

A. Non-small cell lung cancer

TTF-1 (thyroid transcription factor 1) is a protein which regulates the transcription of genes specific for the thyroid and lung. Lung adenocarcinomas and small cell carcinomas are usually TTF-1 positive. The histology in the above example is suggestive of an adenocarcinoma and therefore this is mostly likely a lung primary given the TTF-1 stain and history of smoking.

Non-small cell lung cancers include adenocarcinoma, large cell and squamous cell carcinoma.

Question 21 of 43

A 76-year-old woman with metastatic transitional cell carcinoma of the bladder is admitted to hospice with a 3-day history of hallucinations, confusion and pruritus. Her only other symptoms are intermittent vomiting and pelvic discomfort. She has a past medical history of hypertension and has recently completed a course of radiotherapy for bone metastases. She takes paracetamol, morphine sulphate, cyclizine, dexamethasone and a herbal flower remedy for anxiety.

On examination, she is cachectic and frail. The lungs are clear and heart sounds are normal. Pulse rate is 85 beats per minute and blood pressure 130/80mmHg. She is afebrile.

Neurological examination reveals myoclonus. She is mildly hypotonic and all reflexes are diminished. There is miosis on cranial nerve examination.

Blood tests show:

Hb	12.1 g/dl
Platelets	250 * 10 /l9
WBC	12 * 10 /l9
Na +	135 mmol/l
K +	4.3 mmol/l
Urea	5 mmol/l
Creatinine	80 µmol/l
Calcium (unadjusted)	2.1 mmol/l
Bilirubin	15 µmol/l
ALP	45 u/l
ALT	15 u/l
AST	20 u/l
Albumin	28 g/l

Urine dip: no abnormality What is the most likely diagnosis?

A. Hypercalcaemia
B. Opioid toxicity
C. Sepsis
D. Corticosteroid psychosis
E. Brain metastases

B. Opioid toxicity

This lady is presenting with opioid toxicity. She has vomiting, confusion, hallucinations and pruritus. Her symptoms have been precipitated by a reduction in her opioid requirement. This is a common occurrence in patients who have radiotherapy for bone metastases if their medication dose is not adjusted.

Hypercalcaemia could cause a similar presentation, but the corrected calcium is 2.4 mmol/L. This lady is hypoalbuminaemic due to her advanced cancer. The patient no symptoms of infection. She is apyrexial and her slightly raised white cell count is due to her advanced disease and dexamethasone treatment. Corticosteroid psychosis is possible, but would not cause the neurological signs or pruritus. Transitional cell carcinomas of the urothelial tract only rarely metastasise to the brain; the neurological signs suggest opioid toxicity rather than a focal lesion.

Question 22 of 43

A 65-year-old man is referred to the oncology team after presenting to the emergency department. The patient described a three-week history of progressive thoracic back pain. The pain was localised to a point between the patient's shoulder blades, and was exacerbated by movement and coughing.

In addition, over the previous 6 hours, the patient reported that he had been struggling to stand up unassisted, and was having difficultly walking. The sudden change in his mobility had been the event that had prompted his attendance at hospital. When questioned directly, the patient described intermittent tingling sensations in his lower legs, but denied any loss of sensation. There had been no dysfunction of his bladder or bowels.

The patient had been diagnosed with prostate cancer five years previously. This had been treated with a radical prostatectomy and hormone therapy. The patient had moved area two years previously, and had subsequently been lost to urological follow-up. Despite his previous cancer treatment, the patient stated that he was very fit and active, playing golf three times a week and taking an active role in the care of his grandchildren.

Peripheral nerve examination of lower limbs: tone generally increased bilaterally; power generally slightly reduced (4+/5) bilaterally; normal coordination; no impairment of light touch or sharp touch sensation; knee and ankle jerks brisk bilaterally, plantar responses up going bilaterally.

Digital rectal examination: preserved peri-anal sensation and normal tone. Bed-side bladder scan: 50 ml

MRI whole spine: metastatic invasion and collapse of T10 vertebral with spinal cord compression.

The patient was treated with analgesia and dexamethasone while definitive treatment was planned.

What is most appropriate first-line treatment of patient's spinal cord compression?

A. Surgical tumour resection and spinal cord stabilisation with adjuvant radiotherapy
B. Radiotherapy: single dose 8 Gy
C. Chemotherapy: docetaxel
D. Best supportive care
E. Chemotherapy: cabazitaxel

A. Surgical tumour resection and spinal cord stabilisation with adjuvant radiotherapy

The best predictor of neurological outcome with treatment in metastatic spinal cord compression is neurological status at the initiation of treatment. The patient in the question has presented very promptly and has only limited neurological compromise. Therefore, it is imperative that definitive treatment is provided promptly (ideally, within 24 hours) to optimise long-term outcome.

Definite treatment of metastatic spinal cord compression can include any combination of radiotherapy, surgery and chemotherapy. Recent evidence indicates that surgery is superior to radiotherapy in retaining or regaining neurological function and relieving pain. In the case of this patient, who has an excellent performance status, surgery followed by radiotherapy would likely offer a better outcome than radiotherapy alone.

Radiotherapy may be considered as first-line treatment in some circumstances. Recommended regimen vary, for example 20 Gy in five daily fractions. The radiotherapy regime offered as a answer to the question would be appropriate as palliative treatment for pain-control, making it an incorrect answer for this patient.

Chemotherapy have a role in the management of spinal-cord compression secondary to chemosensitive malignancies (for example, small-cell lung cancer or germ cell tumours), but would not be optimal treatment for this patient.

Question 23 of 43

A 56-year-old patient presents to hospital with confusion. He is a long-term smoker. He has a past-medical history of chronic

obstructive pulmonary disease, hypertension, bipolar disease and long-term muscular back pain.

On examination he is confused with a Glasgow Coma Scale score of 14 out of 15. He has a pulse rate of 97 beats per minute with a blood pressure of 145/97 mmHg. Respiratory rate is 14 per minute with oxygen saturations of 95% on room air. He has bilateral vesicular breath sounds on auscultation with normal percussion. His abdomen is soft and non-tender with no masses. He has no focal neurology.

Investigations

Hb	102 g/dL
WCC	8.2 *10^9/l
Platelets	133 *10^9/l
Na+	146 mmol/L
K+	5.4 mmol/L
Cr	132 µmol/L
Ur	10.1 mmol/L
Albumin	26 g/L
Adjusted Calcium	3.78 mmol/L
Alkaline Phosphatase	76 IU/L
PTH	Undetectable
Serum ACE	45U/L (10-50)
Serum Electrophoresis	IgG 18 g/L (5-13 g/L) - Polyclonal
Urinary Electrophoresis	Undetectable
Chest X-ray	Right parahilar opacification 3x4cm
Lumbar Spine X-ray	Normal

What is the likely underlying diagnosis?

A. Squamous Cell Carcinoma
B. Multiple Myeloma
C. Sarcoidosis
D. Drug induced hypercalcaemia
E. Prostate carcinoma

A. Squamous Cell Carcinoma

The patient has severe hypercalcaemia. The commonest causes are hyperparathyroidism and cancer. The patient has a normal alkaline phosphatase without evidence of fracture or bone disease making bone metastases unlikely. The patient has a normal serum ACE with an atypical chest X-ray for sarcoidosis, although unilateral chest findings are possible.

The patient has features of multiple myeloma including anaemia, renal insufficiency and hypercalcaemia. However, there is a polyclonal, rather than a monoclonal increase in paraprotein.

The chest x-ray findings with a background of smoking suggest an underlying respiratory malignancy. This patient has squamous cell carcinoma of the lung with parathyroid related protein secretion causing hypercalcaemia. PrPTH is not deteced on a PTH assay. Hypercalcaemia can induce confusion and renal impairment.

Question 24 of 43

A 65-year-old man with metastatic squamous cell lung cancer is admitted to the Acute Medical Unit for the management of hypercalcaemia. He is currently taking slow-release morphine sulphate (MST) 90mg bd to control his pain along with regular naproxen and paracetamol. During his admission he complains of pain in his right arm which is the site of a known skeletal metastasis.

What is the most appropriate medication to prescribe to treat his acute pain?

A. Oral morphine solution 30mg
B. Oral morphine solution 15mg
C. Oral morphine solution 10mg
D. Add alendronate 70mg weekly
E. Tramadol 50mg

A. Oral morphine solution 30mg

This patient is describing break-through pain. Whilst bisphosphonates have a role in bone metastases they are not suitable for acute pain. A suitable break-through dose is therefore 1/6th of the total daily morphine dose i.e. 1/6th of 180mg = 30mg.

Question 25 of 43

A 77-year-old female is electively admitted for investigation of bilateral lower limb swelling onset over the past 3 years associated with limitation of exercise as a result. Her past medical history includes bilateral pulmonary emboli in 2010 and type 2 diabetes mellitus. On examination, nonpitting bilateral lower limb oedema is noted to the high thighs without abdominal involvement. Her heart sounds are normal with no added sounds, her chest is clear. Her abdomen is soft and non-tender without ascites or superficial swelling. A transthoracic echocardiogram demonstrates normal left ventricular function but was unable to produce good views of the right heart. A CT pulmonary angiogram demonstrates no embolus, a ventilation-perfusion scan demonstrates a low probability of pulmonary emboli. Ultrasound abdomen is unremarkable. The patient undergoes a right heart catheter, demonstrating a mean pulmonary arterial pressure of 14mmHg.

What is the likely cause of her lower limb swelling?

A. Left heart failure
B. Idiopathic pulmonary arterial hypertension
C. Right heart failure
D. Pelvic malignancy
E. Lymphoedema

E. Lymphoedema

Interpretation of the various investigations this patient has undertaken allows lymphoedema as a diagnosis of exclusion. The patient would have been referred to this standard set of investigations for pulmonary hypertension after clinically presenting as progressive exercise limitation and peripheral oedema, with the primary concern being right heart failure secondary to an increased pressure within the pulmonary vasculature.

Most importantly, the pulmonary arterial pressure is normal on the right heart catheter, ruling idiopathic pulmonary hypertension. Left heart dysfunction is excluded by a normal echocardiogram evaluation of the left ventricular function. CTPA and normal abdominal ultrasound, predominantly investigating the portal circulation, rule out causes of pulmonary hypertension. Lastly, the non-pitting nature of the oedema suggests a non-cardiac cause, making lymphoedema the most likely cause of lower limb swelling.

Question 26 of 43

A 65-year-old man is admitted to the hospital for palliative radiotherapy. He has a squamous cell carcinoma of the tongue that has metastasized to his neck and surrounds the carotid artery. There are no surgical options to treat his disease.

On day 2 of the admission, he experiences a catastrophic bleed from his neck.

What is the most appropriate medication to administer in this circumstance?

A. Buscopan
B. Chlorpromazine
C. Haloperidol
D. Midazolam
E. Morphine

D. Midazolam

In a massive terminal haemorrhage, a large dose of midazolam (10mg) can be given as part of 'crisis management' to relieve distress. Red or green towels or blankets should be available to soak up and mask the colour of blood

Midazolam is the correct answer. The patient has experienced a terminal haemorrhage as a consequence of his tumour eroding through the carotid artery. Given the lack of surgical options available to treat his condition, urgent symptom control is warranted to manage this distressing event. Intravenous midazolam is indicated in this horrific situation as a consequence of its anxiolytic and sedative effects, along with the rapidity of its onset.

Haloperidol is incorrect. This can be used to treat agitation in palliative care. However, intravenous midazolam is preferred in this catastrophic situation due to its rapidity of onset.

Morphine is incorrect. This is typically used to treat pain and breathlessness in a palliative care setting, rather than agitation.

Chlorpromazine is incorrect. This can also be used to treat agitation in a palliative care setting. However, midazolam is preferred in terminal haemorrhages.

Buscopan is incorrect. This is used to decrease the burden of secretions in palliative care. It is not used to treat agitation.

Question 27 of 43

A 64-year-old Nepalese woman who emigrated to the United Kingdom six months prior arrives to her GP. She has known multinodular goitre which has been untreated. However, her daughter who translates for her reports that she has noticed a tight sensation like she is being strangled. This is worse in the mornings and her daughter has noticed that her face does appear puffy. She has no weight loss, fevers or night sweats. She is otherwise well and has never smoked.

On examination, there is a large multinodular goitre that occupies a large part of the neck and measures 15-20cm in width. There is no audible stridor but there are several neck veins visible. You ask her to stretch out her hands up high to observe for a tremor and she starts to complain of the tightness. becoming worse. Her chest sounds are quiet and her chest is clear. There is dull percussion under the top third of the sternum.

TSH	0.07 mU/L (normal range 0.05-5.0)
T4	10 pmol/L (normal range 9-50)
T3	4.0 pmol/L (normal range 3.5-7.8)
D-dimer	0.15 (normal range 0-0.25)
Chest x-ray	Widened mediastinum, no focal lung lesion

What is the underlying cause of these new symptoms?

A. Multinodular goitre
B. Lymphoma
C. Thoracic artery aneurysm
D. Lung carcinoma
E. Superior vena cava thrombus

A. Multinodular goitre

Enlarged goitre can be a rare cause of SVC obstruction

This presentation is classical for superior vena cava obstruction and the worsening of her symptoms when she lifts her hands up is Pemberton's test which is positive in this case. The next decision is to seek the cause. The obvious cause here is a huge goitre which is recognised as a rare cause of superior cava obstruction. Lung carcinoma is possible but this lady is a non smoker and there is no cough or weight loss. Thoracic artery aneurysm would show a widened mediastinum but there would often be a history of connective tissue disease or uncontrolled hypertension. Lymphoma causing SVC obstruction would typically have mediastinal lymphadenopathy on chest x-ray. SVC thrombus would be unlikely given that the D-dimer is negative

Question 28 of 43

A 78-year-old gentleman with known metastatic prostate cancer is admitted due to lower back pain that is worse on sitting upright. He denies any sensory changes or weakness but is woken at night and cannot sleep. He takes aspirin, paracetamol and bicalutamide regularly.

On examination, he has normal tone, full power and downgoing plantars in both lower legs. He is exquisitely tender in the midline at L2 and L3.

Bilirubin	34 µmol/l
ALP	450 u/l
ALT	56 u/l
Albumin	32 g/l
Calcium	3.1mmol/l
MRI spine	sclerotic lesions seen in T9, L2 and L3

What medical therapy would offer greatest benefit to him?

A. Intravenous fluids
B. Denosumab
C. Spinal decompressive surgery
D. Omeprazole
E. Transcutaneous electrical nerve stimulation (TENS)

B. Denosumab

Denosumab is an unlicensed medication for bony metastasis pain

This gentleman has bony pain associated with bony metastases. This is a key question in identifying the problem and how to help him. There is no sign of nerve compression so spinal surgery will not benefit him. He is asymptomatic from his hypercalcaemia so

IV fluids would not benefit. Omeprazole will help protect his stomach from ulceration. For bony pain, NSAIDs usually are a good first line. Bisphosphonates and radiotherapy help but are not an answer. Denosumab is a third line when the above fail. TENS can be useful for all pains but is not evidence based for bony pain.

Question 29 of 43

You are fast-bleeped to the oncology ward to review a 72-year-old man with a background of metastatic, fungating buccal cancer. During initial MDT, it was deemed inoperable due to carotid artery involvement. He was initially admitted with hypercalcaemia but has deteriorated during his admission and is on the end-of-life pathway.

On your arrival, you note a large amount of blood around the patient with staff using towels and applying pressure to the neck. Nursing staff report that there was a sudden 'pop' and large volume bleeding began at the site of the fungating cancer. They state that bleeding has occurred before but not to this extent.

What is the most appropriate next step in management?

A. Adrenaline
B. Midazolam
C. Morphine
D. Terlipressin
E. Vascular surgery opinion

B. Midazolam

In a massive terminal haemorrhage, a large dose of midazolam (10mg) can be given as part of 'crisis management' to relieve distress. Red or green towels or blankets should be available to soak up and mask the colour of blood

This is an example of a catastrophic, terminal haemorrhage likely arising from carotid artery involvement. In these circumstances, patients can become very distressed and unfortunately, often there is very little that can be done. To aid in relieving stress it is advised to use red or green towels to help soak up blood as well as obscuring the colour of the blood, as well as giving a large dose of midazolam for relaxation.

Adrenaline can be used in specific circumstances of major haemorrhage but is not used in terminal haemorrhage. Given that the history explains that the patient is on the end of life pathway and that he is not for surgical intervention, adrenaline is not appropriate.

Morphine can be used for pain and breathlessness in palliative care but is not used in terminal haemorrhages.

Terlipressin can be used for major haemorrhage, particularly of gastrointestinal bleeding, however again, this is not appropriate in terminal haemorrhages.

The MDT has already decided that surgical intervention is not appropriate and therefore a vascular surgery opinion at this time would not be appropriate.

Question 30 of 43

A 60-year-old woman presented to the emergency department with recurrent episodes of severe headache and vomiting over past 3-4 days. She was known to have underlying metastatic breast cancer for which she was receiving palliative chemotherapy. She was also known to have underlying type 2 diabetes mellitus and osteoarthritis of bilateral knee joints.

On examination, her pulse rate was 105/min, respiratory rate was 16/min, blood pressure was 120/80 mmHg. Fundoscopy revealed early papilloedema.

A contrast enhanced CT brain was done which showed a solitary mass of 3 cm in the left cerebral hemisphere.

What is the next appropriate management?

A. Start 16 mg of i.v dexamethasone and prophylactic anticonvulsants
B. Start 16 mg of dexamethasone and arrange urgent MRI brain
C. Refer to neurosurgery for biopsy of the brain lesion
D. Refer to radiation oncologist for Whole brain radiotherapy
E. Stereotactic radiosurgery

B. Start 16 mg of dexamethasone and arrange urgent MRI brain

High dose dexamethasone is the mainstay of immediate management of brain metastasis. For lesions identified as solitary on contrast enhanced CT brain, MRI with gadolinium is indicated to assess the extent of intracranial disease. Patients presenting with seizure activity should be given anticonvulsant therapy. Patients with limited number of lesions(<4) can be considered for more aggressive treatment like neurosurgery or stereotactic radiotherapy but not the immediate step. Biopsy of the lesion is indicated if primary is unknown.Whole brain radiotherapy is indicated for multiple brain metastasis (>4).

Question 31 of 43

A 48-year-old woman is currently undergoing various cycles of chemotherapy for breast cancer. She asks the oncology team for advice as, 2-3 days post-chemotherapy, she experiences severe nausea and vomiting that lasts for several days. This is debilitating, despite taking antiemetics during the chemotherapy and afterward.

What is the most appropriate drug to prevent this delayed reaction?

A. Dexamethasone
B. Levopromazine
C. Lorazepam
D. Metoclopramide
E. Ondansetron

A. Dexamethasone

Dexamethasone is the most useful agent in preventing the delayed phase of chemotherapyinduced emesis

Dexamethasone has been shown by numerous trials to be the most effective agent in preventing delayed nausea and vomiting. As opposed to more immediate nausea and vomiting, for which

antiemetics are useful, the delayed reaction (between 24 hours and 1-week post-chemotherapy) is not as effectively reduced by antiemetics.

Levopromazine is a 'dirty drug', acting at multiple receptor sites. It is a useful antiemetic, particularly parenterally, but sedates patients quite significantly and is generally reserved for palliative care and intractable symptoms.

Lorazepam, a benzodiazepine, has mild antiemetic properties and is not considered effective at reducing the delayed phase. It is generally used for its anti-anxiolytic properties.

Metoclopramide is a dopamine antagonist and an effective antiemetic. It may be used first-line for immediate nausea and vomiting. However, in the context of the delayed phase, dexamethasone is more useful.

Ondansetron is a serotonin receptor antagonist and another effective antiemetic used for chemotherapy-induced nausea and vomiting. With regards to the delayed phase, however, dexamethasone is the most effective agent.

Question 32 of 43

A 68-year-old man with metastatic prostate cancer is due to go for radiotherapy in an hour. The nurses tell you that he complained of pain during the transfer yesterday. His pain has been otherwise well controlled on a total of 60mg morphine daily.

How is it best to manage his pain control for the transfer today?

A. Nothing as it is only temporary pain
B. An additional dose of 10mg morphine 30 minutes prior to his transfer
C. An additional dose of 15mg morphine 1 hour prior to his transfer
D. An additional dose of 10mg morphine 1 hour prior to his transfer
E. An additional dose of 15mg morphine 30 minutes prior to his transfer

B. An additional dose of 10mg morphine 30 minutes prior to his transfer

A breakthrough dose of morphine should be given 30 minutes prior to his transfer as indicated in the BNF. 1 hour is too long prior as it should last him the transfer back and 30 minutes prior is enough for the morphine to have the desired effect. A breakthrough dose should be 1/6th of his total daily dose which in this case is 10mg. Therefore, 15mg is too high a dose for this patient.

Although it is temporary pain, it should still be treated as the patient's comfort and quality of life are important aspects of his care.

Question 33 of 43

A 72-year-old man presents to the emergency department with shortness of breath. He describes his breathlessness has progressively become worse over the last two weeks and is especially troublesome when leaning forward. His wife has commented that his appearance has changed too, with his face becoming more swollen and different in colour. He has a past medical history of right-sided heart failure, myocardial infarction, type two diabetes, COPD and small cell lung cancer diagnosed three months ago. He is an ex-smoker of 20 pack-years and drinks moderate amounts of alcohol.

On examination, he appears settled at rest. His face is swollen and slightly purple. His neck veins are distended and his JVP is markedly elevated to 4cm. Auscultation reveals bibasal crepitations. There is pitting oedema at the ankles. A chest X-ray demonstrates a widened mediastinum.

What investigation is most appropriate to establish the diagnosis?

A. ECG
B. Trans-thoracic echocardiogram
C. Trans-oesophageal echocardiogram
D. Bronchoscopy
E. CT chest

E. CT chest

The correct answer is CT chest as the patient has a clinical history consistent with obstruction of the superior vena cava (SVC). There are several symptoms and signs consistent with SVC obstruction, including breathlessness worse, leaning forward, distended neck veins and a swollen face. This, in combination with known lung cancer, suggests progression of the primary malignancy or lymph nodes compressing the SVC. Whilst some of the finds could be suggestive of acute pulmonary oedema, the chest X-ray is consistent with SVC obstruction. As a cardiac cause is unlikely, an echocardiogram or ECG is unlikely to be diagnostic. A bronchoscopy is a possible approach for obtaining a biopsy if an SVC obstruction is diagnosed and the source of the obstruction is unclear, but as this patient is known to have lung cancer this is not going to be helpful for this patient.

Question 34 of 43

A 40-year-old man is seen in the Emergency Department with breathlessness.

He was diagnosed with non-Hodgkin lymphoma 6 months ago and has been receiving chemotherapy. He is awaiting an appointment in haematology outpatients to assess his response to chemotherapy.

He describes becoming more breathless over the last week and feeling that his arms and face are puffy. He has had no chest pain, cough or fevers.

On examination his oxygen saturations are 92% on air and his heart rare is 112 beats per minute. His chest is clear and he is unable to lay flat for his abdomen to be examined due to is breathlessness. His face appears flushed and he has oedema of the arms and hands. His neck veins appear engorged.

Chest x-ray shows a widened mediastinum with extensive lymphadenopathy.

A CT scan of the thorax confirms superior vena cava obstruction (SVCO). The scan is reviewed by the haematology team who explain to him that his lymphoma has progressed despite chemotherapy.

He is started on steroids and a proton pump inhibitor.

What is the next step in the management of this gentleman's SVCO?

A. Chemotherapy
B. Observation
C. Radiotherapy
D. Stent insertion
E. Surgery

D. Stent insertion

SVCO is an oncological emergency and is most common in lung cancer and lymphomas. The immediate management is steroids with proton pump inhibitor cover for gastric protection.

Further options include stent insertion, radiotherapy and chemotherapy.

This gentleman is unable to lay flat so would not be able to tolerate radiotherapy. Radiotherapy also has the disadvantage of causing increased swelling acutely before it causes long term shrinkage.

Lymphomas are highly chemotherapy responsive tumours and this gentleman has only had firstline chemotherapy, therefore second-line chemotherapy should be planned in order to shrink his mediastinal disease.

Stent insertion is the most immediate management for relieving SVCO until chemotherapy can take effect. The patient's haemoglobin, platelets and clotting must be checked and optimised. In patients with end-stage disease, stents can still become blocked.

Surgery is not generally part of the management for SVCO.

Question 35 of 43

A 71-year-old woman is referred by her GP to the rapid access chest clinic with progressive shortness of breath and reduced exercise tolerance over 3 months and a chronic productive cough. When asked about her past medical history she states that she has had some pain for the past month or so in her left shoulder, which has been present at a constant level. She has been taking paracetamol and codeine for the pain which helps slightly. Otherwise, the patient has moderate COPD, for which she taken ipratropium bromide and salmeterol and mechanical back pain. She has a 15 year pack-history and drinks 1-2 units of alcohol per day.

Examination reveals some wasting of the hypothenar eminence of the left hand, although the chest sounds clear bilaterally with no added sounds. Heart sounds 1 and 2 are present with no murmurs.

What would be the most useful investigation following a chest x-ray?

A. Electromyogram studies
B. Computed tomography of the thorax
C. Bronchoscopy
D. Myeloma screen
E. Sputum microscopy, culture and sensitivity

B. Computed tomography of the thorax

The most likely diagnosis in this case is lung malignancy, in particular a Pancoast tumour, given this patient's wasting of the hypothenar eminence, shortness of breath and cough. The most useful investigation is a CT of the thorax - bronchoscopy is not as useful as the cancer is often too peripheral.

Question 36 of 43

You are asked to review a 67-year-old gentleman who was admitted to the medical emergency unit with pneumonia. He had been diagnosed with terminal small cell cancer of the lung which had extensively metastasised to his liver, thoracic vertebrae and femur bones. His past medical history was comprised of ischaemic heart disease, hypertension, hypercholesterolaemia and COPD.

His main complaint was of progressively worsening pain in his spine and legs. This was particularly bothersome at night; a trial of bisphosphonate therapy and radiotherapy did not provide any symptomatic relief. He was commenced initially on oral morphine sulphate solution which was converted to morphine sulphate tablets (MST); he had been on 60mg BD but this was titrated by the palliative care community nurse to 70mg BD a couple of days prior to admission with excellent analgesic effect. He was also using Oramorph solution 10mg on average 5-6 times a day for breakthrough pain.

He had been accordingly treated with intravenous antibiotics whilst on the ward making a full recovery. Prior to discharge, he was very keen on commencing transdermal treatment so as to minimise the number of oral medications taken.

What is the most appropriate starting dose to commence, with a view to completely discontinuing all oral opiate medication?

A. Commence Fentanyl 12 72 hr patch, paracetamol 1g QDS and oramorph solution PRN for breakthrough pain
B. Commence Fentanyl 25 72 hr patch, paracetamol 1g QDS and oramorph solution PRN forbreakthrough pain
C. Commence Fentanyl 50 72 hr patch, paracetamol 1g QDS and oramorph solution PRN forbreakthrough pain
D. Commence Fentanyl 75 72 hr patch, paracetamol 1g QDS and oramorph solution PRN forbreakthrough pain
E. Commence Fentanyl 100 72 hr patch, paracetamol 1g QDS and oramorph solution PRNfor breakthrough pain

D. Commence Fentanyl 75 72 hr patch, paracetamol 1g QDS and oramorph solution PRN forbreakthrough pain

This gentleman was on a rather complicated opiate analgesia regimen and the key to this question is calculate the total daily dose of morphine salt, to then convert it to the appropriate amount of fentanyl.

His total morphine salt intake was thus:

MST 70mg BD = 140mg of morphine Oramorph 10mg PRN = 50-60mg of morphine

Total = 190-200mg daily morphine salt intake

The BNF states that a fentanyl 75 patch is equivalent to 180mg daily intake of morphine salt whilst a fentanyl 100patch is equivalent to 240mg daily morphine salt intake. So as to avoid opiate toxicity the correct answer is thus to commence a fentanyl 75 patch and to supplement this with PRN Oramorph solution.

Question 37 of 43

A 68-year-old man presents with a five-week history of lower back pain that is worse with coughing. He has noticed that he has been requiring more painkillers to the point where he is struggling to manage, especially at night. The pain is worse when straining to pass stool. He lost three kg over the last four months as well. He has a past medical history of COPD, hypertension, type two diabetes mellitus, and hypercholesterolemia. He has been admitted three times in the last year for exacerbations of COPD requiring the recurrent use of oral prednisolone. His regular medications include Symbicort, tiotropium, atorvastatin, metformin, paracetamol, codeine and Movicol. He is an ex-smoker with a 50 pack-year history and recently opted for early retirement from his job as an accountant as he was struggling with tiredness. On examination, he appears tired and his clothes appear loose fitting. Examination of his chest is unremarkable, but there is a 1cm swelling above his left clavicle. His abdomen is soft, there is no tenderness over his spine, and a neurological examination is unremarkable.

Observations:

Saturations	95%
Respiratory rate	15/min
Blood pressure	148/87mmHg
Heart rate	74/min
Temperature	37.4°C

Blood tests:

Hb	128 g/l
MCV	72 fl
Platelets	327 * 10 /l9
WBC	12.4 * 10 /l9
Na +	136 mmol/l
K +	4.2 mmol/l
Urea	4.1 mmol/l
Creatinine	77 µmol/l

What is the most likely diagnosis that explains his symptoms?

A. Osteoporotic vertebral collapse
B. Spinal cord metastasis
C. Myeloma
D. Degenerative changes
E. Discitis

B. Spinal cord metastasis

The answer is spinal cord metastasis. This question highlights multiple subtle red flags in a history with back pain. He is over >55 and describes nocturnal and progressive pain worse with coughing and straining in the context of immunosuppression from repeated steroid use, weight loss, and increasing fatigue. Due to the high suspicion, the most diagnostic imaging investigation would be a whole spine MRI, which would differentiate between the above diagnoses. Osteoporotic fracture is suggested by the use of steroids but overall does not fit with the progressive nature and microcytic anaemia, nor do degenerative changes. There are very few symptoms to suggest infection such as fever and night sweats, but discitis cannot be fully excluded without imaging. Myeloma is a possible diagnosis, but so far there are no specific factors to suggest it, such as lytic bone lesions or deteriorating renal function.

Question 38 of 43

A 56-year-old male with non-hodgkin's lymphoma is on his third cycle of R-CHOP chemotherapy. He has struggled previous times with nausea but is two days following the most recent cycle and attended hospital due to intractable vomiting.

He is vomiting 20+ times a day with green to clear fluid. He does not feel hungry and struggles to swallow water. He is not having diarrhoea. He takes regular indapamide and as required ondansetron and this has not helped him despite the oncologist suggesting he double his dose of ondansetron.

On examination, he looks pale and has dry mucosa. He is alert, has a clear chest and soft abdomen but begins to retch on sitting forward. He last passed urine 6 hours ago and his observations show a heart rate of 115 beats per minute and blood pressure 90/65mmHg. He is started on intravenous fluids by the emergency department.

Na +	135 mmol/l
K +	3.5 mmol/l
Urea	6.5 mmol/l
Creatinine	98 µmol/l

What medical intervention would offer greatest benefit?

A. Cyclizine
B. Potassium salt replacement
C. Elective terminal ileostomy
D. Dexamethasone
E. Delay next course of chemotherapy

D. Dexamethasone

Dexamethasone with ondansetron is effective in refractory chemotherapy-induced vomiting

This gentleman has refractory vomiting despite ondansetron. He need assistance to ensure he can maintain fluids. Cyclizine is an antiemetic but bind histamine receptors so is most useful in labyrinthitis and motion sickness. Potassium salt replacement will probably make him vomit more but does replace his lost salts. Delaying the course of chemotherapy would be an option if nothing else could be offered. Surgery is not the way forward here. Dexamethasone is proven as an effective second line antiemetic in chemotherapy related nausea and vomiting. it is often given in lymphoma to prevent tumour lysis syndrome.

Question 39 of 43

A 38-year-old man presents with increasing shortness of breath and ankle swelling. He reports he is more short of breath, especially on exertion, which is not being relieved by the use of his salbutamol inhaler. He has also noticed his ankles are swollen by the end of the day.

His past medical history includes asthma, which is usually well controlled, and lymphoma, which was treated with chemotherapy several years ago. His only medications are his beclometasone and salbutamol inhalers. The results of his blood tests are shown below:

Hb	140 g/L	(135-180)
Platelets	359 * 10 /L 9	(150 - 400)
WBC	7.2 * 10 /L 9	(4.0 - 11.0)
Na +	137 mmol/L	(135 - 145)
K +	4.3 mmol/L	(3.5 - 5.0)
Urea	5.9 mmol/L	(2.0 - 7.0)
Creatinine	119 µmol/L	(55 - 120)

His ECG showed sinus rhythm with left axis deviation. An echocardiogram was done which showed dilation of all four chambers of the heart and a left ventricular ejection fraction of 40%.

Which drug can be attributed to causing this man's presentation?

A. Cyclophosphamide
B. Vincristine
C. Doxorubicin
D. Docetaxel
E. Bleomycin

C. Doxorubicin

Anthracyclines (e.g. doxorubicin) may cause cardiomyopathy

This man is presenting with features of heart failure and the echocardiogram results would be in keeping with a diagnosis of dilated cardiomyopathy. Doxorubicin (an anthracycline) is used in the treatment of lymphoma and is known to be cardiotoxic.

Cyclophosphamide can also be used to treat lymphoma and other haematological conditions such as leukaemia. A well-known side effect is haemorrhagic cystitis.

Vincristine can be used with doxorubicin to treat lymphoma and is associated with peripheral neuropathy.

Docetaxel is often used in the management of breast and lung cancers and can cause neutropenia.

Bleomycin can be used as part of lymphoma management and is associated with the development of pulmonary fibrosis.

Question 40 of 43

You are reviewing a 65-year-old man who has recently started treatment for urological cancer with Nivolumab (Opdivo) a type of checkpoint inhibitor.

He has been having treatment for 1 month and has had no side effects so far. He would like to know what to expect from this treatment.

What is the most common side effect this patient is likely to experience?

A. Dry itchy skin and rashes
B. Depression and anxiety
C. Dry cough
D. Retinal damage
E. Skin discolouration

A. Dry itchy skin and rashes

The most common side effect of immune checkpoint inhibitors is dry itchy skin and rashes

Immune checkpoint inhibitors are a type of immunotherapy that are increasingly being used to treat certain types of cancer, as an alternative to cytotoxic chemotherapy. They are currently only used to treat solid tumours. They work by enhancing the bodies own T-cell population to destroy the cancer cells.

Their side effect profile reflects their mechanism of action and are, therefore, inflammatory and autoimmune in nature. They include:

- Dry, itchy skin and rashes (most commonly)
- Nausea and vomiting
- Decreased appetite
- Diarrhoea
- Tiredness and fatigue
- Shortness of breath and a dry cough.

Therefore, option one is the only correct answer.

Question 41 of 43

A 54-year-old male presents to the emergency department with sudden onset palpitations and shortness of breath which began whilst he was watching television a few hours previously. He describes an odd fluttering sensation in his chest with mild dyspnoea but no chest pain. He denies having experienced this before. On systems review, he also complains of severe muscle cramps and a slight tremor in his hands over the last few days. His past medical history includes hypertension and gout for which he takes amlodipine and allopurinol. He denies any history of exertional dyspnoea but does occasionally get central chest pain on exertion for which he has not sought help. He has recently been diagnosed with small cell lung cancer and underwent his first round of chemotherapy last week; although he is unsure which drugs are being used. He used to smoke a pipe until his recent diagnosis of cancer and drinks a few measures of whisky most evenings.

On examination, his respiratory rate is 22 breaths/min and his oxygen saturations are 96% breathing two litres of oxygen. His heart rate is irregularly irregular and approximately 130 beats/min, his blood pressure is 152/78 mmHg. An ECG shows atrial fibrillation with no ischaemic changes.

What is the most likely cause for his new atrial fibrillation?

A. Ischaemic heart disease
B. Chemotherapy induced hypokalaemia
C. Chemotherapy induced hypomagnesaemia
D. Chemotherapy induced cardiomyopathy
E. Alcohol

C. Chemotherapy induced hypomagnesaemia

The most common chemotherapy regime for small cell lung cancer is etoposide and cisplatin. A common side effect of cisplatin is hypomagnesaemia which can result in muscle cramps, tremor, cardiac arrhythmias, confusion amongst other features. This gentleman appears to have angina and may well have some level of ischaemic heart disease in the background which would increase his risk of atrial fibrillation. However, it seems logical given the strong temporal relationship between the chemotherapy and the other symptoms of hypomagnesaemia that this is the cause.

Question 42 of 43

A 63-year-old man is diagnosed with colorectal cancer. Following successful resection he starts adjuvant capecitabine but after six doses develops severe diarrhoea, weakness and desquamation of the hands, feet and face. On admission, he is pancytopenic and has electrolyte abnormalities requiring IV replacement. His initial blood tests are shown bellow.

Na +	140 mmol/l
K +	3.6 mmol/l
Urea	9.2 mmol/l
Creatinine	125 µmol/l
Hb	75 g/l
Platelets	35 * 10 /l9
WBC	0.4 * 10 /l9
Neutrophils	0.03 * 10 /l9
Adjusted Ca 2+	1.5 mmol/l
Mg 2+	0.32 mmol/l
Glucose	4.0 mmol/l

What is the most likely cause?

A. DPD (dihydropyrimidine dehydrogenase) deficiency
B. Infective gastroenteritis
C. Cancer recurrence
D. Pityriasis alba
E. Neutropenic sepsis

A. DPD (dihydropyrimidine dehydrogenase) deficiency

Capecitabine is the oral analog of 5-fluorouracil, a chemotherapeutic agent which is broken down, predominantly, by dihydropyrimidine dehydrogenase (DPD). Deficiency is autosomal recessive and will lead to a toxin buildup which in homozygous patients is usually fatal. The severe toxicity experienced by this patient are likely due to a heterozygous DPD deficiency.

Question 43 of 43

A 53 year old patient has undergone six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) chemotherapy and is now attending the lymphoma follow up clinic. He complains of an ongoing and unrelenting tingling in his feet and legs as well as his right hand. This is associated with pain in the extremities that is worsened by the cold weather.

Examination reveals normal motor strength throughout all 4 limbs but marked reduction in proprioception in both legs below the knee and also the right hand. The is a 'glove and stocking' distribution of loss when tested for pin-prick sensation and a reduced joint position sense to the ankle in both lower limbs. Plantar reflexes are normal. During the examination you it is noted that the patient has sustained an injury to the sole of foot which he was unaware of.

What is the most likely causative agent for these symptoms?

A. Rituximab
B. Cyclophosphamide
C. Doxorubicin
D. Vincristine
E. Prednisolone

D. Vincristine

The symptoms being experienced above are classical for chemotherapy induced peripheral neuropathy. This is a condition that can occur in up to 40% of patients being given chemotherapy with agents such as platinum based drugs (cisplatin and oxaliplatin), vinca alakloids (vincristine and vinblastine), thalidomide and taxanes (paclitaxel and docetaxel). The treatment of chemotherapy induced peripheral neuropathy is difficult with patients having severe problems long after the causative agent has been given. In most cases it is irreversible. The best medication for treatment is gabapentin or pregabalin which should be titrated up to therapeutic levels and used in conjunction with another analgesic agents.

There are ongoing trials aiming to find a prophylactic agent to help prevent this painful sequealae of treatment, but as yet there has been no convincing evidence to suggest any one treatment.